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"STUDY OF CLINICAL PROFILE AND EFFECT OF GLYCOLIC ACID, SALICYLIC-MANDELIC ACID AND PHYTIC ACID COMBINATION CHEMICAL PEELS IN MELASMA"

Submitted By

Dr Sheraun Karira

2020-2023

GUIDE

Dr VK Garg

Prof &Head Of Department

Department of Dermatology, Venereology & Leprosy

Santosh Deemed to be University

No. 1, Santosh Nagar, GHAZIABAD-201009, NCR, INDIA

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Guide

Dr**. VK Garg**

Professor & HOD

Department of Dermatology, Venereology & Leprosy

Santosh Medical College & Hospital

Ghaziabad (U.P.), India

CERTIFICATE BY THE HEAD OF THE DEPARTMENT

This is to certify that the thesis titled **"Study of clinical profile and effect of Glycolic acid, Salicylic-Mandelic acid and Phytic acid combination chemical peels in melasma"** is a bonafide research work carried out by **Dr. Sheraun Karira** in partial fulfilment of the requirements for award of the degree of M.D. Dermatology, Venereology & Leprosy.

PROF. (Dr.) VK Garg

M.B.B.S., M.D.

Professor & Head

Department of Dermatology, Venereology & Leprosy

Santosh Medical College & Hospital

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This is to certify that the thesis titled **" Study of clinical profile and effect of Glycolic acid, Salicylic-Mandelic acid and Phytic acid combination chemical peels in melasma "** is a bonafide research work carried out by **Dr. Sheraun Karira** under the esteemed guidance of **Dr. VK Garg** Santosh Medical college and is presented before the ethical committee of Santosh University, Ghaziabad for requisite approval.

Dr Alka Agrawal

Dean

Faculty of Medical Sciences

Santosh Medical College & Hospital

Santosh University

Ghaziabad – 201001 (U.P.)

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INTRODUCTION

Melasma, derived from the Greek word “Melas’’ means “Black” is a common acquired hyperpigmentation of skin seen over face and uncommonly on neck and forearms.[1] Melasma, formerly known as chloasma, is an acquired pigmentary condition, occurring most commonly on the face. This disorder, which is more prevalent in females and darker skin types, is predominantly attributed to ultraviolet (UV) exposure and hormonal influences. It’s incidence is more in females as compared to males but clinical and histological features are similar.[2] Women make up for 90% cases of melasma.[3] Overall prevalence ranges widely at 1–50%, since values are typically calculated within a specific ethnic population within a geographic region. Some studies on melasma suggested the prevalence in male varied from 10% (Puerto Rico) to 25.8% (India).[4] It has been reported more in darker complexion individuals of skin type IV to VI as defined by Fitzpatrick. [5] The mean age of onset being 29.99 years, ranging from 14 to 54 years.[6] Multiple etiologies, including light exposure, hormonal influences, and family history, have been implicated in the pathogenesis of this disorder. Etiology of melasma is unknown but sunlight and genetic factors play an important role. Some of the other factors responsible for melasma are pregnancy, oral contraceptives, thyroid dysfunction and various drugs like Phenytoin.[7]

Melasma is generally a clinical diagnosis consisting of symmetric reticulated hypermelanosis in three predominant facial patterns: centrofacial, malar, and mandibular [7]. The major clinical pattern in 50–80% of cases is the centrofacial pattern, which affects the forehead, nose, and upper lip, excluding the philtrum, cheeks, and chin [8,9]. The malar pattern is restricted to the malar cheeks on the face, while mandibular melasma is present on the jawline and chin. The latter is thought to occur in older individuals and may be more related to severe photodamage [10]. A newer pattern termed extra-facial melasma can occur on non-facial body parts, including the neck, sternum, forearms, and upper extremities [11]. Though common, the management of this disorder remains challenging given the incomplete understanding of the pathogenesis, its chronicity, and recurrence rates. In addition to traditional treatments for melasma, there are also promising new treatments, including topical, oral, and procedural therapies.

Morphologically, melasma presents as symmetric reticulated hyperpigmented patches with irregular borders on the centrofacial region, malar cheeks, mandible, and rarely upper chest and extremities. While melasma is known to more commonly affect darker skin types, it can occur in all skin types [8,9,12]. There are 3 clinical patterns namely centrofacial, mandibular and malar. It has been classified into epidermal, dermal, mixed and indefinite type by the Woods lamp.[6] Recently a non invasive technique, dermoscopy has been used to classify melasma as dermal, epidermal and mixed on the basis of location of pigment and talengiectasia.[13]

On dermoscopic examination, it is possible to see pronounced hyperpigmentation in the pseudo-rete ridges of the skin [7]. Using a Wood's lamp, the hyperpigmentation can be accentuated when the pigment is epidermal [6]. However, this accentuation may be seen with dermal or mixed melasma [1,14]. The differential diagnosis for melasma includes lichen planus pigmentosus, discoid lupus erythematosus, phototoxic dermatitis, erythema dyschromium perstans, phytophotodermatitis, pigmented contact dermatitis, drug-induced pigmentation, poikiloderma of Civatte, erythromelanosis follicularis faciei, ochronosis, hori's nevus, argyria, nevus of ota, lentigines, ephelides, macular amyloidoses, and post-inflammatory hyperpigmentation [15]

Various modalities of topical and systemic treatment are available. The commonly used topical agents are hydroquinone, azelaic acid and kojic acid.[16] Various type of chemical peels such as Glycolic acid, Salicylic acid, Mandelic acid, Phytic acid and their combinations have been used for the treatment of melasma. There are few studies comparing Glycolic acid, Salicylic- Mandelic acid and Phytic acid combination peels as melasma is more common in darker complexion individuals where they have higher tendency of developing pigmentary changes, less amenable to the chemical peels.[17]
In one such study Salicylic-Mandelic acid definitely appeared to be a promising therapeutic tool as compared to Glycolic acid and Phytic acid combinations in Indian patients.[17] Hence to further strengthen this hypothesis present study was undertaken.

LACUNAE IN EXISTING LITERATURE

There is paucity of literature comparing the efficacy of Glycolic acid, Salicylic-Mandelic acid, Phytic acid combination peels in melasma.

AIMS AND OBJECTIVE

1. To study clinical profile of melasma patients using modified MASI score and Dermoscopy.

2. To study the effect of Glycolic acid, Salicylic-Mandelic acid and Phytic acid combination chemical peels in melasma.

REVIEW OF LITERATURE

Epidemiology

Various epidemiologic studies have estimated the prevalence of melasma in the general population at 1% and in higher-risk populations at 9–50% [18–21]. These wide ranges are secondary to variations in prevalence among darker skin types, different ethnic heritages, and different levels of UV exposure within various geographic locations. As such, the true prevalence across the entire population is unknown. The age of onset is also unknown, with average age ranging being between 20 and 30 years [3,8]. One study argued that patients with mandibular melasma have an older age of onset in their 40s[4]. Many studies have attempted to calculate the prevalence and incidence of melasma from data available in dermatology clinics. However, this approach may underestimate the number of affected individuals given that some patients with milder disease may forgo clinical evaluation, as well as the potential for misdiagnoses.

A prospective telephone-based study in a com-munity of Latino women in the southwestern United States found a prevalence of 8.8% amongst 500 interviewed individuals [20]. Another prospective study on melasma prevalence in a New York City dermatology private practice found a prevalence of 8.2% amongst 1000 Latino patients [22]. Globally, the prevalence of melasma has also varied. A study of 3298 people in Saudi Arabia revealed a 2.9% prevalence, compared to a prevalence of13.4–15.5% seen in an Arab-American population in Michigan [23,24]. Additionally, a retrospective study in a health center in Ethiopia demonstrated a 1.5% prevalence [25]. Studies have shown that melasma has a female predominance [6,8,26]. Although the general accepted female to male ratio is 9:1, amore recent large, multi center study of 953 melasma patients in Brazil found a 39:1 ratio [6,26]. An Indian study of 312 patients with melasma found a 4:1 female to male ratio [8]. During pregnancy, the prevalence likely increases, which was seen in a cross-sectional study in Tehran with a 15.8% prevalence amongst pregnant women. Similarly, in a randomly selected sample of 2000 pregnant women in India, there was a 50.8% prevalence[12,13]. Fewer studies have been carried out on men with melasma, but they clinically tend to exhibit similar clinical features and exacerbating factors [27]. Two major risk factors found in Indian and Latino men include sun-exposure and outdoor work [27,28].

Pathogenesis

The etiology of melasma is multifactorial. UV light has been shown in clinical and laboratory studies to trigger and exacerbate the condition [8]. UV light is thought to induce reactive oxygen species (ROS) by activating inducible nitric oxide and promoting melanogenesis [29].Patients with melasma have also been found to have higher markers of oxidative stress when compared to healthy volunteers [30]. More recently, the role of visible light in inducing pigmentation has been appreciated. A seminal study showed sustained pigmentation from visible light in darker skin types over 2 weeks compared to pigmentation from UVA-1 light [31]. Another study showed that visible light at a wavelength of 415 nm can cause increased pigmentation that could last for 3 months [32]. The process of melanogenesis after UV and visible light exposure can be stimulated by keratinocytes and fibroblasts. One major pathway of both UV- and visible light-induced pigmentation is the secretion of stem cell factor (SCF),the ligand for the tyrosine kinase receptor, c-kit, which leads to downstream effects on the proliferation of melanocytes [33]. A recent study showed the increased expression of SCF in the dermis and c-kit in the epidermis in areas of melasma [33]. This is further supported by increased mRNA levels of melanogenesis-associated genes [34]. Other studies have found increased levels of Wnt signaling-related genes, which is notable since Wnt has been linked to the proliferation of melanocyte stem cells[34,35]. Additionally, vascular endothelial growth factor (VEGF), a product of keratinocytes after UV damage, can sustain human melanocytes in tissue culture [36]. This is pro-posed as one of the mechanisms for the increased activity of melanocytes in melasma[36,37]. Recent gene and protein expression studies have also shown down-regulation of lipid metabolism-associated genes in lesional skin, which may suggest impaired barrier function as contributing to the pathogenesis of melasma [34].Family history is also known to be an important risk factor for developing melasma, strengthening the hypothesis of a genetic pre-disposition to the condition. Some studies have reported that 55–64% of patients with this condition have a positive family history[18,38,39]. No genome-wide study has been performed to examine associated genes, but current findings would suggest that the genes responsible involve pigmentary, inflammatory, hormonal, and possibly vascular responses. Patients with Fitzpatrick skin type (FST) II and III are less likely to have a positive family his-tory than patients with darker skin types (IV–VI)[6,40].Hormonal influences play a significant role in the pathogenesis of melasma as seen by the increased prevalence with pregnancy, oral contraceptive use and other hormonal therapies[2,3,39,40]. Extra-facial melasma has also been associated with a

peri-menopausal state [5,6].An immunohistochemical study of the epidermis and dermis of affected and unaffected neighbouring skin found significantly increased expression of the progesterone receptor in the epidermis of affected skin [41]. There was also increased estrogen receptor protein expression in the dermis and around the blood vessels, which is currently of unknown significance[42]. Melasma has not been consistently associated with other clinical conditions. In a case–control study, melasma was shown to be associated with an increased number of lentigines and nevi [38]. Endocrinological conditions, such as thyroid disease, have also been investigated as having an association with melasma, but observed prevalence of thyroid diseases in these studies are not increased when compared to the general population [8,43].Histology Historically, melasma has been classified as having three histologic variants: epidermal, dermal, and mixed [1]. In the epidermal type, there is increased pigment throughout the layers of the epidermis, particularly in the basal and suprabasilar layers. Melanocytes in the epidermis are generally enlarged, have prominent dendrites, and increased melanosomes[9,44]. Although one study suggested an increase in melanocyte number, most studies report no change in the number of epidermal melanocytes [44]. Epidermal pigmentation maybe accentuated with a Wood's lamp which may help distinguish epidermal and dermal sub-types. The dermal subtype has melanophages in the superficial and deep dermis. Additionally, a lymphohistiocytic infiltrate may be seen in the dermis in areas with increased melanin deposition. Dermal findings can also include solar elastosis and an increase in blood vessels [9,11].Mixed melasma often displays combined histologic features of the epidermal and dermal subtype.

Clinical Assessment and Psychosocial Implications

Given the variability of presentation, assessing melasma severity can be challenging. Several validated tools have been created to evaluate both the clinical appearance and the psychosocial impact of dyspigmentation from melasma. Moreover, these standardized tool shave enhanced the ability to assess therapeutic efficacy of various melasma treatments in clinical trials. The Melasma Area and Severity Index (MASI) is a validated scale used to measure the extent of facial hyperpigmentation. This is anumeric score calculated as an area-weighted score of pigmentation and homogeneity located on the forehead, chin, right and left malar cheek [39]. After eliminating homogeneity from the calculation due to the decreased interrater reliability of that metric, the modified MASI (mMASI) was created [45]. It has now been correlated to the Melasma Severity Score, which is a global score that incorporates both objective data and patient's subjective assessment. It is now used in clinical trials [46] For

many dermatologic conditions, a health-related quality of life (HRQoL) tool has been used to measure the psychosocial aspects of skin diseases. Balkrishnan and colleagues created the Melasma Quality Of Life Scale(MELASQOL), a validated modified version of the HRQoL [47]. The scale consists of 10 ques-tions pertaining to the quality of life and impact of the disease rated on a Likert scale. Other psychometric scales that can be used in those with melasma are the Dermatology Life Quality Index (DLQI) and the SKINDEX-16 [48–52].

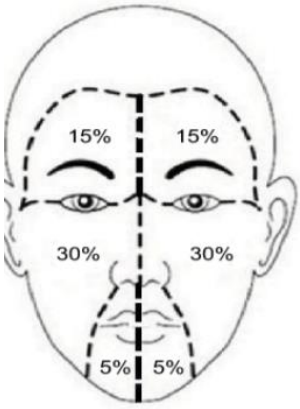
The modified Melasma Area and Severity Index (mMASI)

Melasma Area and Severity Index (MASI) is the most widely used outcome measure in clinical studies on melasma. [53,54] MASI score, proposed by Kimbrough-Green *et al*. in 1994, has been devised on the pattern of Psoriasis Area and Severity Index (PASI). [55] Interestingly, MASI uses an almost similar formula for the face as is used for the whole body in PASI score. Moreover, the three variables of area, induration, and scaling in PASI are replaced by area, pigmentation, and homogeneity in MASI score. [55] While the variables of "pigmentation" and "area of involvement" are certainly important to consider in melasma the fallacy lies in how these variables are applied in MASI.

The Melasma Area and Severity Index (MASI) is the most common outcome measure used for melasma studies, and was validated 20 years after it was first reported.[53,54] This validation process eliminated homogeneity as a part of the MASI, resulting in the new modified MASI score (mMASI).[54]

Calculation of the mMASI score is performed by rating darkness and area of involvement of 4 areas of the face. These figures are then inserted into an equation, resulting in the final mMASI score (Figure 1).

Kimbrough et al devised melasma area severity index (MASI) score to provide more accurate quanitification of severity of melamsa.[55] The MASI score is calculated by subjective assessment of area (A) of involvement, darkness (D), and homogeneity(H) with the forehead (F), right malar region (MR), left malar region (ML) and chin (C), corresponding to 30%,



Modified MASI scoring

Frontal	15%
Malar	30%
Chin	5%

0.15(A)(D+H)+0.3(A)(D+H)+0.05(A)(D+H)

Score: range: 0–24

Area	Darkness
0=no involvement; 1=<10; 2=10–29; 3=30–49; 4=50–69; 5=70–89; and 6=90–100	0=absent; 1=slight; 2=mild; 3=marked; and 4=severe

30%, 30% and 10% of the total face respectively. Each of the 4 areas is given a numeric value of 0 to 60 = no involvement; (1 = <10% ; 2 = 10%-29% ; 3 = 30%-49% ; 4 = 50-69% ; 5 = 70%-89% ; 6 = 90%-11%). Darkness and homogeneity are rated on a scale of 0-4. (0 = absent; 1 =slight; 2 = mild; 3 = marked; and 4 = maximum). MASI is calculated by adding the sum of the severity rating for darkness and homogeneity, multiplied by the value of the area of involvement, for each of the 4 facial areas.
MASI total score = 0.3A(F)[D(F) + H(F)] + 0.3A(ML)[D(ML) + H(ML)] + 0.3A(MR)[D(MR)+ H(MR)] + 0.1A(C)[D(C) + H(C)].

In a study by Pandya et al it was stated that measurement of darkness and area was sufficient in determining severity of melasma, whereas homogeneity was unreliable and should be eliminated from MASI, as a result of this a modified MASI score was devised. [56]

Modified MASI score = 0.3A(F)D(F) + 0.3A(ML)D(ML) + 0.3A(MR)D(MR) + 0.1A(C)D(C).

In a study by Sarkar R et al on 90 Indian patients of melasma where group A was treated with 35% GA peel, group B was treated with SM peel(20%SA-10%MA) and group C was treated with Phytic acid combination peel, it was observed that the change in MASI score in group A was 62.6% and 39.38% at 12 and 20 weeks respectively, in group B change in MASI score was 60.98% and 41.67% respectively whereas in group C change in MASI score was 44.71% and 28.27% at 12 and 20 weeks respectively. [48]

WOODS LAMP :

Wood's light emits an ultraviolet A light through it's woods filter which is opaque to all

radiation except those to a wavelength between 320-400 nm.[57] It is the most widely used method to classify melasma. However it predominantly penetrates the stratum corneum and epidermis and does not help much in picking up the dermal component of melasma. Another established disadvantage being that this technique is not useful in individuals with skin type V and VI due to optical factors.[58]

DERMOSCOPY:

Dermoscopy is a non invasive and in-vivo diagnostic tool which visualises subtle patterns of clinical structures not visible to the naked eyes. It was introduced in 1920 by German dermatologist Johann Saphier, but Goldman was the first person to use it for pigmentary lesions.[59] It is used to assess the level and pattern of pigmentation of melasma. Melanin pigment appears as dark brown with well defined network when present in stratum corneum. Shades of light brown with an irregular network is seen when located in lower epidermis whereas blue or bluish grey colour when located in the dermis. It also helps greatly to monitor treatment efficacy, pick up talengiectasia's and to differentiate it from exogenous ochronosis which worsens with hydroquinone treatment.[60] Few studies that have been done to classify melamsa by dermoscopy are described below in table 1.

TABLE 1

AUTHOR	PATIENT NUMBER	CLINICAL CLASSIFICATION	DERMOSCOPY
Nanjundaswamy et al [60] Karnataka Dharni et al [61] Maharashtra	100 patients of melasma 80 patients of melasma (70 female and 10 male patients)	Clinical classification : 47% patients belonged to the centrofacial type melasma and 53% patients belonged to the malar type melasma Clinical classification : 47.5% were found to have centrofacial pattern, 38.75% had	On dermoscopy : 46% patients showed epidermal type of pattern (scattered islands of brown reticular network with fine granules scattered on surface), 18% patients revealed a dermal pattern (uniform skin involvement, no areas of

		malar pattern and	sparing with dark brown to grey hyperpigmentation) and 36% patients showed a mixed pattern(feature of both epidermal and dermal) On dermoscopy : 57.5% had epidermal type(light brown with regular pigmented network), 36.52% had dermal type(grey brown with irregular network) and 6.25%

Through this table we conclude that in the following studies of melasma through dermoscopy epidermal melasma has varied from 40-57.5%, dermal melasma has varied from 18%-36.52% whereas mixed type of melasma has varied from 6.25 -37.5% and that brown colour with regular pigmentation has been observed in epidermal type melasma, grey with irregular pigment network in dermal type melasma and patterns of both types in mixed melasma.

VISUAL ANALOG SCALE (VAS) : It is used for measurement of the treatment response. In a study by Garg K et al the patient, treating physician and an independent observer made a subjective assessment of the response on a 5-point visual analog scale: Worse, no change, poor (<30%), fair (31-60%), good (>60%). [62]

In a study by Nourmohammadi et al VAS has been used to assess improvement in melasma lesions of patients being treated with hydroquinone and fractional CO2 laser vs hydroquinone monotherapy, on the side treated with combination of laser and hydroquinone, satisfaction with treatment increased from 4.66±3 to 6.6±2, which showed a statistically significant change (P=0.002). On the side treated with hydroquinone, the value increased from 4.44±3 to 5.7±2, which was a statistically significant (P=0.005). [63]

Tamler et al Rio de Janeiro 2021 [13]	40 patients of melasma	13.75% had mandibular pattern Clinical classification : 24 patients had centrofacial, 14 malar, 3 mandibular and 3 had extrafacial melasma	had mixed type melasma (presentation of areas compatible with both) On dermoscopy : 40% had epidermal type(brown with regular pigmented network), 22.5% had dermal type(bluish grey with irregular network) and 37.5% had mixed type melasma (presentation of areas compatible with both)

Treatment

Treatments for melasma include topical, oral, procedural, and combination treatments. These are aimed at various aspects of the pathogenesis of melasma including photodamage, inflammation, vascularity, and pigmentation (Table).

Topical

Topical treatments, including photoprotection, are typically the first-line therapies for melasma. The most common therapeutic agents used are those that inhibit the production of melanin through melanogenesis and melanocyte proliferation. Concomitant use of various topical therapies with different mechanisms of action are preferred to monotherapy.

Modality	Treatment	Mechanism of action	Adverse effects (AE)
Topical	Iron oxide	Block visible and ultraviolet light	Irritation
	Hydroquinone (HQ),	Tyrosinase inhibitor	Irritation, exogenous ochronosis (with HQ)
	Azelaic acid,		
	Ascorbic acid,		
	Kojic acid		
	Tretinoin	Increased keratinocyte turnover	Irritation, redness
	Corticosteroids	Anti-inflammatory with non-selective inhibition of melanogenesis	Telangiectasias, epidermal atrophy, steroid-induced acne, striae, hypopigmentation
	Ascorbic acid	Inhibition of reactive oxygen species	No significant AE
	Niacinamide	Inhibition of melanosome transfer	Irritation
Oral	Tranexamic acid	Inhibits plasminogen/plasmin pathway → inhibition of melanin synthesis	Abdominal bloating, menstrual irregularities, headache, deep venous thrombosis
		Decreases vascular proliferation	
	Polypodium leucotomos, Glutathione	Inhibition of reactive oxygen species	No significant AE
Procedural	Q-switch ruby laser,	Melanosome destruction	Burn, post inflammatory pigment alteration (PIPA)
	Q-switch Nd:Yag laser		
	Non-ablative fractional lasers	Fractional photothermolysis leading to melanin extrusion	Burn, PIPA
	Chemical peels	Increased keratinocyte turnover	Burn, peeling, PIPA
	Microneedling	Transdermal drug delivery	Erythema, edema, tram-track marks, PIPA
	Intense pulsed light	Extrusion of melanosomes	Burn, PIPA
	Radiofrequency	Cellular biostimulation	Burn
		Transdermal drug delivery	

AE adverse effects, *HQ* hydroquinone, *PIPA* post-inflammatory pigment alteration, *Nd:YAG* neodymium-doped yttrium aluminum garnet

Table 1: Melasma treatment modalities, their mechanism of action and adverse effects.

Photoprotection

UV and visible light avoidance are critical to prevent flares and exacerbation of melasma. In repeated randomized-controlled studies with40–60 subjects, a comparison of broad-spectrum UVA and UVB filters combined with visible light blockers, such as iron oxide, versus broad-spectrum UV filters alone showed reduced melasma relapses in the former group[64–66].

Hydroquinone

Hydroquinone (HQ) has historically been the most studied topical agent in the treatment of melasma. This compound works by inhibiting tyrosinase, which prevents the conversion of DOPA to melanin [67]. Others have postulated that it can also directly lead to melanocyte destruction and melanosome degradation. In several studies, the use of HQ 4% has led to a statistically significant improvement of melasma dyspigmentation [68]. Although very effective and dosed at different strengths, it can cause an irritant dermatitis in some individuals and chronic use can lead to exogenous ochronosis [7].

Corticosteroids

Corticosteroids can prevent pigmentation by non-selective suppression of melanogenesis while also serving as an anti-inflammatory agent [69]. Corticosteroids alone are unlikely to be superior to depigmenting agents when used as monotherapy [69]. Although they have an independent ability to suppress melanogenesis, the current literature shows that corticosteroids have not been demonstrated to have long-term benefits in treating melasma [67]. Moreover, long-term steroid use may lead to telangiectasias, acne, epidermal atrophy, striae, and hypopigmentation.

Retinoids

Topical retinoids have also been effective intreating melasma, with a postulated mechanism of promoting keratinocyte turnover [70]. A small but sentinel study in 1993 showed that tretinoin 0.1% cream could significantly decrease objective colorimetry measurements of melasma pigmentation [70]. Another study has confirmed the beneficial use of tretinoin 0.1% cream for the treatment of melasma in Black patients [71].

Other Synthetic Topical Compounds

Another tyrosinase inhibitor, 4-n-butylresorci-nol, has been increasingly used in trials and has shown significant improvement in pigmentation in melasma [72,73]. Noted adverse effects, including erythema and pruritus, were self-limited and minimal; however, long-term data on this product is lacking. Tranexamic acid, a synthetic version of lysine and a hemostatic agent, has been increasingly used in the topical, oral, and injectable forms to treat melasma. Studies have demonstrated occasional negative findings when used as a monotherapy, but increased efficacy when used in combination with other pigmentation-based therapies [70–78]. The topical formulation of tranexamic acid, however, has had limited success and less

efficacy than when used in oral form. Topical flutamide, an antiandrogenic agent, has also been studied in comparison to HQ 4%, and was found to have statistically significant MASI scores and patient satisfaction; however, no difference in the mexameter melanin assay was observed between the two groups [79].

Natural Topical Compounds

In recent years, naturally occurring compound shave been investigated for their therapeutic activity against pigmentation. Niacinamide, which inhibits melanosome transfer to keratinocytes, has been shown to decrease pig-mentation in a small study with 27 subjects[80]. Both ascorbic acid and kojic acid can inhibit tyrosinase activity and have been shown in small studies to lead to decreased pigmentation [80–82]. Ascorbic acid has a theorized benefit of decreasing reactive oxygen species, which decreases inflammation in melasma lesions [29,82]. However, both were shown to be inferior to HQ in improving MASI scores when used as monotherapies [57,58,83].Another natural compound, azelaic acid (AA),was noted in an open-label study to be effective in improving pigmentation by inhibiting tyrosinase activity [49]. This compound, which is derived from the yeast, Pityrosporum ovale, also has anti-inflammatory effects. Adverse effects are not common, but can include burning and erythema. Bellis perennis, a flower extract that inhibits melanin synthesis, was demonstrated, in combination with topical licorice and emblica, another natural antioxidant, to be similar in efficacy to HQ 2% in decreasing pigmentation and inhibiting inflammation through the arachidonic acid cascade [84]. Other topical natural compounds used, such as lignin peroxidase, arbutin, and soy, have also been used to treat melasma in small studies with favorable results [80, 85–87].

Combination Topical Compounds

Recent studies have shown that combination topical therapies are superior to monotherapies in efficacy [88]. Triple combination therapy (TCT) with HQ, a retinoid, and a topical steroid was the first combination topical therapy to gain United States Food and Drug Administration approval. In an investigator-blinded randomized study with 260 Asian patients, TCT with HQ 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01% was superior to HQ 4% monotherapy in improving melasma [89]. Of note, about 50% of patients on TCT reported increased erythema, skin irritation, and discomfort when compared to 14% of controls. Dual therapy with tretinoin 0.1% and HQ 3%was also demonstrated to improve melasma among female Korean patients [90].Camouflage With the recurring nature of melasma and the long,

challenging treatment duration, cosmetic camouflage can provide patients with another option to improve the psychosocial effects of the condition and quality of life. Cosmetic camouflage, including concealers and other pigmented cover-ups, has been shown to significantly improve the DLQI in a study of 24patients with pigmentary disorders [91]. Several cosmetics brands offer pigmented foundations and concealers that may even skin complexion and may also include broad-spectrum UV blockers.

Oral

In addition to topical therapies, oral therapies are emerging as additional treatment options for this disorder. Tranexamic acid (TA), an anti-plasmin agent, decreases the generation of arachidonic acid, which leads to a reduction in melanocyte-stimulating hormone (MSH) and a decrease in pigmentary production [77]. One study showed that TA may also decrease VEGF and entothelin-1, both of which may be responsible for increasing vascularity in affected lesions [50]. While formulations of tranexamic acid have not been directly compared, recent studies generally suggest that about 90% of patients treated orally improved after 2–-6 months compared to about 95% of patients treated with topical 2% preparations and who improved after 3 months [50,77,78]. Notable adverse effects of oral TA include abdominal bloating, headache, tinnitus, menstrual irregularities, and, rarely, deep venous thrombosis (DVT) [77]. Due to the serious risk of a DVT, screening for risk factors of thrombosis is necessary before initiating treatment. Alternative medications, such as Polypodium leucotomos (PL) and glutathione, have also been studied as adjunctive treatments with positive results [92–94]. PL has been shown to decrease UV-induced photodamage and inhibit ROS, which in turn decreases the T cell-mediated response that leads to increased inflammation and pigmentation in the skin [93]. In a randomized controlled trial in the Philippines, oral glutathione, a naturally occurring compound, resulted in decreased melanin when compared to those taking placebo over a 4-week period[94]. Glutathione is thought to act as an anti-oxidant that decreases inflammation [80].

Procedural

The recent literature on procedural melasma therapies has predominantly included case reports and case series that evaluate the use of chemical peels, microneedling, microderm abrasion, and lasers, typically in conjunction with other treatment modalities. It is important to note that many procedural studies include concomitant use of topical therapies and photoprotection [37,95–99].

CHEMICAL PEELING:

Chemical peeling is a technique used to improve the appearance of the skin. A chemical solution is applied to the skin, which causes it to separate, peel off, and allows new skin to regenerate. The new skin is smoother and less wrinkled than the old skin, and may also be more even in color Dermatologists have used various peeling agents for decades and are experts in performing all types of this chemical surgery. This concept dates back to Roman times. Superficial and medium depth skin peeling with trichloroacetic acid has been a well documented therapy in United states since atleast 1960. Dr. Baker and Gordon pioneered chemical peeling with phenol in the year 1961. Chemical peeling one of the latest treatments available for the about disease in modern era. Superficial and medium depth skin peels can create dramatic improvement in the skin but the results were not long lasting as those with phenol peels. The use of retinoic acid alpha hydroxyl acids, broad-spectrum sunscreens and skin bleaches as part of a post-peel maintenance programme has allowed patients maintain the improvement in skin for far longer.[100]

Chemical peeling is basically an accelerated form of exfoliation induced by the use of a chemical cauterant or escharotic agent. Very light peeling agents induce a faster sloughing of the cells in the stratum corneum where as deeper peeling agents create necrosis and inflammation in the epidermis, papillary dermis or reticular dermis.[100]

History of chemical peels: The first breakthrough in histological assessment of chemical peeling was perhaps by Brown and Kaplan, who demonstrated thickening of dermis in rabbit ears treated with phenol, a phenomenon they termed Fibrosis In 1985, Kligman modified Baker's technique and undertook a long term evaluation of chemical peels. He noted a white band of thin compact collagen bundles arranged horizontally parallel to skin surface, usually 2-3 mm wide. Numerous elastic fibers parallel to collagen bundles were seen. Telengiectasia was noted in the deeper dermis where the peel had not reached.

Mechanism of action:

Stimulation of epidermal growth through removal of stratum corneum [100] Destruction of specific layers of damaged skin.

Induction of an inflammatory reaction deeper in the tissue than the necrosis induced by the peeling agent. It is able to induce production of new collagen and ground substance in the dermis. Epidermal wounds are capable of inducing deposition of collagen and glycosaminoglycans in the dermis.

Wound Heeling

Stages in chemical peeling:

- Coagulation inflammation.
- Re-epitheliazation.
- Granulation tissue formation.
- Angiogenesis.
- Collagen remodeling.

1. **Coagulation inflammation**

These are the initial phases of wound heeling in chemical peeling.. Soluble factors are elaborated in clotting that activate kinins and complement inflammatory pathways, which function as chemoattractant for neutrophils, macrophages and lymphocytes. Macrophages direct the subsequent development of granulation tissue and lymphocyte augment fibroblast accumulation and proliferation.[101]

2. **Re-epithelialization**

This begins within 24 hours of wound-healing. Certain mediators released during inflammation such as fibronectin, laminin and platelet derived growth factor may stimulate keratinocyte cell movement. Fibronectin stimulates adhesion of fibrin, collagen and a variety of cells. The water content of wound-bed is a major factor in the epithelial cell migration rate. Occluded wounds re-epithelialize faster than open dry wound.[102-103]

3. **Granulation tissue formation**

Granulation tissue is a loose collection of cellular components including fibroblast, fibronectin, inflammatory cells, glycosaminoglycans and collagens. Granulation tissue formation begin on second or third day after peeling.[104-105] The

chief cell is the fibroblast which produces fibrillar collagen, elastin , fibronectin and proteases such as collagenases.

4. **Angiogenesis**

After chemical peeling the resumption of blood flow is essential for supplying oxygen and nutrients to the heeling wound.[106-107] Angiogenetic growth factors may be important which are released from fibroblasts, macrophages and endothelial cells.

5. **Collagen remodeling**

Collagen and matrix remodeling begin when granulation tissue formation begins and continues for months after re-epitheliazation.[108] As collagen is laid down, fibronectin gradually disappears. Fibers of collagen type 1 and 3 close together as water is resorbed and reorient in a parallel fashion to the skin surface. This remodeling is responsible for the texture of the skin after peeling.

Fitzpatrick's Classification of skin types :

Skin Type	Color	Reaction to sun
I.	Very white or freckled	Always burn
II.	White	Usually burn
III.	White to olive	Sometimes burn
IV.	Brown	Rarely burn
V.	Dark brown	Very rarely burn
VI.	Black	Never burn, always tan

Classification of peels: [109]

- Very superficial
- Superficial
- Medium depth
- Deep

1.Very Superficial

It is more of an exfoliation. The most superficial layers of the stratum corneum (at the top of the epidermis) [110] is removed or thinned during exfoliation. Most chemical peels have pre-operative regimen of using exfoliating agents. This helps the chemical peeling agents penetrate more deeply and evenly. They have the beneficial property of smoothing out thickened rough area.

Chemicals used are:

30% Lactic acid

Salicylic acid 20% single coat.

TCA 10% single coat

Glycolic acid 35 % 1-2 mins.

2.Superficial

Extend up to the whole thickness of epidermis. They also help reducing the appearance of very mild blotchy skin discoloration, remnant acne discoloration and help cleanse the face.[111]

This is the most common form of skin peel and requires 2-3 days of exfoliation and heeling.

The peeling agents are:

1.TCA 15-20% two coats

2.Glycolic acid 35-50% 2-5 mins.

3.Jessner's Peel.

3.Medium Depth

This is up to the mid dermal level [112]. These agents will cause destruction up to papillary dermis with or without inflammation thus improving superficial scars and rhytides.

Chemical agents used are:

TCA 35-50 % till deep uniform frosting seen.

Glycolic Acid 65-75%

4. Deep Peels

This is up to reticular dermis level. These agents are not advised for Asian skins (type 4 and 5) as there are very high chances of scarring and other complications.

Chemicals used are :

Phenol 88%

TCA 50%

Factors determining depth of peels:

- Peeling agents.
- Concentration of agent applied.
- Number of coats applied.
- Techniques of application
- The manner in which the skin was cleaned and degreased before the peel.
- The method of priming of skin before the peel.
- Duration of contact with the skin.

Peeling for Asian skins:

Deep peeling is not advisable as it causes scarring and hyper or hypo pigmentation in the Asian skin. Even medium depth peel should not exceed 15-20% of TCA and 35% GA. Combination peel or cryopeel can be tried for them. Superficial peels are very safe and cosmetic results are excellent for Indian skin. cryopeel is very useful in treating active acne lesions and superficial scars of acne.[109]

Various peeling agents used are:

Retinoic acid Jessner's solution. Resorcinol Alpha hydroxyl acids. Salicylic acid. Trichloroacetic acid. Phenols.

ALPHA HYDROXY ACIDS (AHA): These are a group of organic acids that have recently become popular in the treatment of a variety of skin conditions, particularly those characterized by hyper keratinisation. Several of these acids are derived from fruits, so they are often referred to as fruit acids.

Glycolic Acid is derived from sugarcane, citric acid from citrus fruit and malic acid from apples [110] the various alpha hydroxy acids are Glycolic Acid, Malic Acid, Mandelic Acid, Lactic Acid, Pyruvic Acid [111] and Tartaric Acid.

Points concerned on using AHA products:

All AHA products may create transient stinging when first applied to the skin. This is normal and not a cause for concern. Persistent stinging longer than 60 seconds implies too strong the product for the patient's skin. It is best to start the patient on low level products and gradually increase the concentration of products. Patients on AHA should use a broad spectrum sunscreen on the morning to protect the newly improved skin. Patients on AHA's usually build up a tolerance to any irritation they may initially experience.

GLYCOLIC ACID PEELS:

Formula: Highest cosmetic grade is a 70% solutions solutions are made using water or a combination of water alcohol and propylene glycol.[112]

Stability: Not light sensitive.
So it does not need to be stored in a dark bottle.
Very stable (more than 2 years)
Deliquescent (absorbs moisture from the air).

Physical Characteristics:
Clear solution can be made to a gel with addition to a gelling agent.
For daily regimen – 8-15% concentration is used. As Peeling Agent: Used in a concentration of 30% or greater.

Advantages:

Even very superficial glycolic acid peels may achieve significant effects.

Systemically safe, non-toxic acids.

They have few complications and well tolerated by patients.

It is an office procedure.

Disadvantages:

There is a tremendous variability from patient to patient in reactivity and efficacy. It has to be neutralized. It has a tendency to penetrate unevenly.

Neutralization: Glycolic acid peels need to be neutralized to terminate their action when they have achieved the desired depth of wound. If they are left un-neutralized, they may penetrate too deeply and over peel the patient. Neutralization can be done using any product with an alkaline PH or by flushing the area with water and diluting the acid. Sodium bicarbonate solution can be used as the neutralizing agent.

Sodium Bicarbonate Solution:

Sodium bicarbonate solution creates carbon dioxide seen as bubbling or fizzing on the surface of the skin. The drawback to sodium bicarbonate solution is that it must be applied in copious amounts to the entire peeled area.

Strength of peel: Starts with 30% and gradually increased to 50% and then 70% to produce a more aggressive peel .

Time of contact:

There is no definite endpoint to AHA peeling.[112]

The stages of glycolic acid in increasing order of depth of peel are:

pink, red, epidermolysis and vesiculation, frosting. Erythema corresponds to intra epidermal wounding. Epidermolysis shows as Grey-White color in areas in which the epidermis is separated from dermis.

Vesiculation is due to epidermolysis.

Frosting seems to be an indicator of dermal injury.

Light AHA peels: Endpoint is mild erythema. Medium depth peels: Endpoint is epidermolysis.

Post Peel Care:
If the patient has any irritation, erythema or superficial crusting after the peel. The daily AHA products or retinoic acid should not be applied. If significant inflammation is present a mild topical steroids cream can be applied twice daily to speed up resolution. If there are areas of crusting it should be treated with a topical anti bacterial ointment. If the patient feels tight or sensitive bland emollient should be applied daily. Areas that can be peeled with glycolic acid: Face commonly, neck , chest and dorsa of hand.

Frequency of Peeling: The superficial peels should be performed with atleast a two weeks interval and 3-4 weeks interval for deep peels.

SALICYLIC ACID:

Introduction:
Salicylic acid has been a main stay in dermatology for many centuries as a topical agent to treat skin disorders. It is also known as beta hydroxy acids. It is a white crystalline powder derived from Willow bark, winter green leaves and sweet birch. Kligman has described salicylic acid as beta hydroxyl acids.

Formula: Salicylic acid – USP 50% Methyl salicylate – 16 drops. Aquaphor – 112 grams.

Physical characteristics:
Lipid soluble. It interacts with lipids that surround keratinized cells there by producing the required keratolytic effect.[113] Salicylic acid must be formulated at a proper PH to allow enough free acids to be present. Thus effective formulations are those in which PH is closer to PKa of 2.98 .

Advantages: Technically easy to perform.[114] Have a low incidence of significant complications. Does not penetrate too deeply. Effective for treatment hyper pigmented age spots on the hands and arms. Comedolytic and lipophilic can be used in acne. Currently a popular component of many in office peels.

Disadvantages:
Have a long healing time.[114] Salicylism is fairly common.

Areas that can be applied:
Face commonly, Arms and hands. Frequency of peeling: Re-peeling should be done with an interval of 2-3 weeks to allow the skin to heal. Concentration of peel used: 20% and 30% salicylic acid are the most common in office peels used.[115]

Action of salicylic acid on acne: BHA is lipophilic—so penetrates the sebaceous material in hair follicle and exfoliate the pores. BHA has strong comedolytic activity.[116] Increases collagen synthesis.

Frosting in salicylic acid peel:
Frost seen in a BHA peeling represents precipitated salicylic acid, while the frost in TCA peel represents precipitated skin proteins. BHA peels frost in 2 minutes. Retouching the frosted areas of TCA peel could result in burning and discouraged.[117] But retouching in BHA peel don't do any harm.

Neutralization: No neutralization for salicylic acid is needed.

Comparison of AHA and BHA:46

	AHA	BHA
Useful in photo-aging	Yes	Yes
Useful in acne [48,56]	Yes	Yes
Useful in Melasma	Yes	Yes
Useful in dry skin	Yes	Yes
Enhances exfoliations	Yes	Yes
Lipophilic	No	Yes
Inhibits arachidonic acid	No	Yes
Anaesthetic properties	May be	Yes
Must be neutralized	Yes	No
Visible frost	No	Yes
Risk of salicylism	No	Yes
Use in pregnancy/breast feeding	Unknown	No
FDA approved for home use	No	Yes
Shown to increase collagen synthesis	Yes	No

PHYTIC ACID

Introduction

Phytic acid or phytate is a naturally occurring alpha-hydroxy acid (AHA), its chemical name is Inositol hexakisphosphate and is present mainly in cereal grains, fibers, and plants. It is a natural plant antioxidant. In recent years, its use in skincare products has increased because of its excellent efficacy and safety profile.

An interesting fact about phytic acid is that it is a chelator, meaning it holds the ability to absorb (or chelate) certain minerals; this may seem to be a disadvantage at first but is indeed a blessing in disguise when it comes to skincare. In general, minerals are essential for good health, but specific ones can have a negative impact on the skin when they become too abundant. Phytic acid absorbs iron molecules in the skin, which are to be blamed for causing damage to the body's DNA.[118]

Phytic acid is a mild Alpha-Hydroxy Acid which has a plethora of benefits, ranging skin moisturizing, wrinkle reduction to deep chemical peeling of the skin.
It acts by promoting exfoliation in our skin and speeding up the natural skin cell rejuvenation cycle. AHAs are known to improve skin texture and reduce the signs of ageing by promoting cell shedding in the outer layers of the skin and by restoring hydration.

Preparations:

- **Oral** – It is an iron chelator and has a strong binding ability (directly or indirectly) to minerals, protein and starch, thereby reducing their intestinal absorption.

- **Topical**– It has both antioxidant & exfoliating properties. It is commonly incorporated in skincare products for its antioxidant properties to help fight sun damage, reduce pigmentation and treat issues like melasma. The mild exfoliating properties along with its potency to clear the pores can be beneficial for those who have a sensitive skin and often face acne breakouts, as it gently clears the skin, shrinks the pores and also adds a brightening glow.

- It is available as phytic acid or IP6 (inositol hexaphosphoric acid) only but in different concentrations, ranging from 0.5% to 5% depending on the use. The more the concentration, the more is its exfoliating ability.

The higher concentrations are used for pigment lightening, anti-aging and exfoliating effects; it is a very mild exfoliant hence higher concentrations are suitable if one is looking to use phytic acid products for it's exfoliating benefits.
Lighter concentrations are used for antioxidant, moisturizing, skin brightening and soothing effects. [119]

Advantages

Phytic acid, being a mild AHA is very safe to use in skin care products as a stand-alone product or in combination with other ingredients. Depending on the concentration, the

benefits that it offers vary; at mild concentration, its antioxidant property makes it a very soothing agent, offer moisturizing effect and allow for a lower pH formulation.

- **Helps acne, open pores and clogged skin**: Calcium settles on the skin surface when it is exposed to hard water, this leads loss of moisture or the skin's ability to hydrate itself, which in turn results in enlarged pores, dry skin, acne and rosacea. Phytic acid absorbs excess calcium on the skin surface, which prevents pores from being clogged thereby reducing breakouts. It also reduces the appearance of pores and stubborn marks on the skin.

- **Anti-ageing benefits**: Owing to its antioxidant property, it acts as a free radical scavenger, hence repairing the skin and preventing oxidative damage to the skin. Our skin is exposed to air pollution, UV rays and other harmful factors on a regular basis, in such a scenario it becomes essential to have ingredients on the shelf that can prevent such damage.

- **Fights Free Radicals:** It prevents havoc-creating molecules from damaging your body and skin. Free radicals are molecules that have lost an electron. These radicals search through your body for the pair. The antioxidant properties of phytic acid contribute one electron to these molecules and prevent them from damaging your skin.

- **Reduce melasma and scarring**: It induces shedding of the dead skin cells and increases cell turnover, which results in lightening pigmentation and scarring.[120]

Mechanism of action

When consumed orally, one major drawbacks of phytic acid is its chelating property. Chelating agents are chemical compounds that react with metal ions to form a stable, water-soluble complex. However, it is beneficial when applied topically as its calcium chelation reduces calcium ion concentration in the epidermis and causes cell desquamation, thereby providing exfoliating benefits. It neutralizes minerals such as iron and calcium present in water that can cause damage to the skin. [121]

Duration of usage

As a stand-alone, since it is a mild exfoliating agent, it will take time to show results in case of pigmentation and wrinkles. So adequate counselling of the patient by a dermatologist is important to ensure that the cream/serum will have to be continued for at least 8-12 weeks. Though results will be visible in 4 weeks with adequate sun protection in the day. The best part about phytic acid is that it suits all skin types including people with extra sensitive skin, this is because of its antioxidant and soothing properties.

Side Effects

This ingredient rarely shows any kind of side effect has been reported with Phytic acid. It is the mildest of all AHAs and safe to be used by people with sensitive skin or acne.
Slight irritation and dryness may be experienced in cases where the ingredient or base used in combination is not suitable for one's skin type.[122]

Interaction with other Ingredients

Phytic Acid has a low pH level at higher concentrations, hence it’s very difficult to combine it with different ingredients. Depending on the formulation that has to be made, it can be neutralized with NaOH 50% and then other ingredients can be made compatible with it. As a stand-alone product phytic acid is not so common, it is usually available in combination with other active ingredients which work synergistically like:
Glycolic acid: Works synergistically in causing exfoliation, phytic acid helps to soothe the skin in case of any irritation caused by glycolic acid.
Azelaic acid/ Butyl resorcinol /Tranexamic acid/ Niacinamide: When used with either of these ingredients, phytic acid helps in better absorption of the other ingredient it is used with.
Salicylic acid: In anti-acne formulations, this combination increases cell turnover and prevents formation of comedones.
Be cautious while using phytic acid with retinol-based applications as it may cause irritation and even nullify the effect of each other.

Phytic acid is a proprietary combination peel containing glycolic, lactic, mandelic, and phytic acid. It is a self-neutralizing, slow-release peel, thus eliminating any risk of overtreatment and need of external neutralization. [123]

Phytic acid combination peel (50%) is a slow release commercial proprietary product. To the best of our knowledge, there are very few studies comparing the efficacy of GA with combination peels like salicylic-mandelic (SM) acid and phytic acid in treatment of melasma. This study will compare its response with glycolic and salicylic–mandelic acid peels.

Phytic acid combination peel has a slow release promoting continuous penetration of the skin, requires no external neutralization and therefore the danger of over peeling is avoided. It allows progressive and sequential actuation of its acid and is non-aggressive. Phytic acid (2%–4%) has proven to be efficient in the treatment of epidermal melasma, especially when associated with GA or retinoic acid. The typical burning sensation seen with the glycolic peel is not observed with the phytic acid peels.

The peeling action of Phytic acid is similar in effect to the more popular glycolic acid but does not need neutralization after application. It is a slow-release agent, allowing progressive actuation of its acid and is non-aggressive when compared with Glycolic Acid. Phytic acid has been shown to be an effective chemical peel agent for the treatment of melasma and acne.[124]

Phytic acid, when used in combination with Glycolic acid, lactic acid, and Mandelic acid offers a variety of benefits. It was observed that the burning sensation felt with glycolic acid was not experienced when it is combined with Phytic Acid.[125]

Other peeling agents:

Trichloro acetic acid:

Advantages: No systemic toxicity.[126]

Can be used to create superficial, medium or deep peels. Inexpensive. Stable. No need to neutralize TCA peel.

Disadvantage: Higher concentrations seem to create scarring.

Concentration used: Up to 20% for Indian skin as concentration more than this can cause pigmentary changes, hyper or hypo pigmentations.

Jessner's peel solution:

Formula: Resorcinol 14 grams, Salicylic acid 14 grams, Lactic acid 14cc, Ethanol to add up to 100cc. [127]

Advantages: Very difficult to over peel a patient and inadvertently create too deep wound. Jessner's peel creates a good deal of exfoliation.

Disadvantages: Greater chance of manufacturing variations. Possible toxicity from salicylic acid and resorcinol.

BASIC CONCEPTS OF CHEMICAL PEELING:

Pharmaceutical considerations:[128]

Peel should be standardized. Variation of factors such as skin type and biological response is inevitable in peels. Legal standards: When chemicals are used in preparations USP grade material should be used. For drugs not listed in USP, national formulatory(NF), British Pharmacopoeia(BP) can be used.

Priming:

Priming the skin for a peel is one of the most important concepts in chemical rejuvenation. The goals of skin preparation are as follows: Reduced wound healing time.50 Priming agents daily for atleast 2 weeks speed up re-epithelization by about 24 hours. Thinning of the stratum corneum by the priming allows better penetration of the peeling agent. Decrease the risk of post inflammatory hyper pigmentation by enhancing the dispersion of melanin granules throughout the epidermis.50 Establish patient compliance and eliminate inappropriate patients.

Agents commonly used to prime the skin for peels include: Retinoic acid, AHA's, Hydroquinone, Kojic acid and Broad spectrum sun screeners.

Bleaching agents can be used for priming in patients with dyschromias. [129]

Chemical peels have been studied as an adjunctive treatment modality for melasma due to their ability to increase epidermal remodeling and to increase keratinocyte turnover. Chemical peels are frequently used in combination with other topical products [130]. Several

studies have suggested that superficial peels may be beneficial for the epidermal-subtype of melasma [130,131]. Amongst the various peels, glycolic acid (GA) has been most extensively studied in the treatment of melasma.

A small open-label study found that 30–50% GA peels at3-week intervals for 6 months in addition to AA20% twice-daily regimen resulted in superior MASI scores when compared to AA 20% alone[132]. However, a small split-face study found no difference in decreased pigmentation when using HQ 4% with GA 20–30% compared to HQ alone [130]. Another split-face study showed no difference in a regimen with salicylic acid (SA)20–30% peel and HQ 4% compared to HQ monotherapy [128-130]. Combination peels have also been explored in recent studies. A study in India found that a combination of 20% SA and 10% mandelic acid was equally as efficacious as 35% GA over12 weeks in significantly improving MASI scores for FST IV and V patients [125]. Trichloro acetic acid (TCA) 10–20% peels were shown to have similar efficacy to GA peels but with more adverse effects, such as burning and peeling[131].

Indications for chemical peel:

1. PIGMENTARY DYSCHROMIAS

- Melasma
- Lentigenes
- Ephelides
- Post inflammatory hyperpigmentation

Epidermal pigmentation responds better to treatment than with mixed or dermal pigmentation.

2. ACNE

- Acne vulgaris
- Acne excorie
- Post acne scarring
- Post acne hyper pigmentation

Superficial peels for acne work primarily through comedolysis and epidermolysis as pustules are unrooted.[121] A series of superficial peels can give dramatic improvement in active acne over a very short period of time.52 Patients with acne tend to have skin very sensitive to peeling.[124-126]

The best can be demonstrated in case of acne excorie.[130] Even in single sitting comedones can be effectively reduced. Post acne pigmentation and scarring can also respond to chemical peels but more number of sittings would be required for the same.

3. ACTINIC DAMAGE AND FINE LINES:

There was statistically significant improvement in rough texture, fine wrinkling an decreased number of actinic keratoses in a study with 50% glycolic acid gel performed by Newman et al.[132]

4. MACULAR AMYLOIDOSIS: Macular amyloidosis has been subjected to chemical peels along with cryotherapy to attain medium depth injury with good cosmetic results.

5. PERIORBITAL PIGMENTATION: As the skin around the eyes is thinner and lax low concentration peels should be used and gradually increased. A lighter peel on the face can have a beneficial additive effect.

METHODOLOGY:

Chemical peeling procedure can be easily divided into 3 steps.

- Pre-peel: preparing the skin for peel
- Peel: actual peel
- Post peel: After care.

Pre peel

Counselling is a very important part of chemical peeling. The patient must be informed about the problems encountered during post peel period, the number of peels to undergo to obtain maximum cosmetic results.

Consent form: Any patient undergoing the procedure should sign a consent form. Written information about the type of peel they undergo. A consent form describing the risk and benefits of the procedure.

Priming: Priming of the skin should be done before the peel as mentioned elsewhere.

Peel

All patients selected for chemical peel must be asked to come :

a. Without any makeup

b. after 2 weeks of using the priming agent.

On arrival to the clinic, the patient must remove contact lens if used Wash all the makeup with soap and water. Wear loose cloths.

Cleansing

The skin should be degreased with cleansing agent such as alcohol, acetone or another agent.

Actual procedure Ask the patient to lie down for facial chemical peel at an angle of 45 degree to prevent pooling of the chemical into the eyes during procedure. Put cotton plugs into the ears. Apply petrolatum to the sensitive areas. put cap on head covering the hair. Eyes closed throughout the procedure. Syringe filled with normal saline in case of accidental spilling into eyes.

Application :

The cotton tipped applicator is tipped in chemical. Eyes closed and peel applied with smooth strokes unit wise and sequentially starting with

a) forehead

b) right cheek

c) left cheek

d)chin

e) nasal bridge, nose , perioral area

f) upper and lower eyelids (least sensitive to most sensitive area)

Feathering the solution in hairline, eyebrow, vermillion and submandibular border done.

Reaction : Erythema , blanch – frost with TCA and salicylic acid. Erythema , epidermolysis with glycolic acid. Terminate the procedure by washing with water till the burning or stinging sensation stops. Don’t cross over eyes during procedures.

Post Peel:

Salicylic Acid: Brownish black pigmentation seen and the skin starts peeling and separates from second day onwards. More the exfoliation better the results.

Glycolic Acid: Erythema may persist for 24-48 hours. Patient looks near normal in the post peel period.

Advice for patients during the healing phase:

To avoid sun exposure.

To avoid exercise.

To avoid having the shower spray strike directly on the face. Not to rub, pick and or unnecessarily touch the face.

To try to sleep on their back.

Complications:

1. Tears drippling on to the neck.[133]

Dripping of the tears on the face causes dilution of acids due to the aqueous solution in the tears. Dripping on to the neck causes an area of peeling on the neck.

2. Premature peeling:

The layer of necrotic skin functions as a protective bandage and premature removal of this layer exposes layer of immature and fragile tissue. This can lead to infection, persistent erythema, post inflammatory hyper pigmentation and scarring.

3. Infections:

The evidence of infection increases with depth of peel. The organism that create infection with peels include:

Common bacterial pathogens –

Staphylococcus and streptococcus species.

Uncommon bacterial pathogens –

pseudomonas and Enterobacter species.

Herpes simplex Candida species.

4. Acne form eruptions:

Appears as multiple tender erythematous follicular papules. They respond promptly to anti biotic therapy used to treat normal acne. Ecchymosis. Small number of patients develop ecchymosis in infra orbital area. These are self limited complications and discoloration resolves completely within 4-6 weeks.

5. Post inflammatory hyper pigmentation:

This is commonly associated with dark skin patients. This gradually improve with time with no therapy except sun avoidance. Broad spectrum sun screeners is mandatory.

6. Hypo pigmentation
7. Allergic reactions.
8. Persistent erythema.
9. Scarring.

CHEMICAL PEELS :

Few studies to study the effect of chemical peels have been done for melasma, as listed below in Table 2.

Table 2 Literature evidence of efficacy of peels in melasma

Author/year	Peel agent	Study group	Methodology	Outcome
Sarkar R et al, [17] Faghiti et al Iran [134]	Group A-35% GA peel Group B-SM peel(20%SA-10%MA) Group C-Phytic acid combination peel Group A	90 Indian patients of melasma 42 female patients with Melasma	Fortnightly superficial peel for 6 peels after priming for 2 weeks with tretinoin Fortnightly superficial peel for 5 peels	Decrease in MASI score in all 3 groups but statistically significantly lower in Group A than Group C (p = .00), significantly lower in Group B than Group C (p = .00),

	Solution of Azelaic Acid (20%), Resorcinol (10%) and Phytic Acid (6%). Group B GA Peel (50%)			no statistically significant difference between Groups A and B (p = .876). MASI score decreased in both groups, whereas in group A score decreased from 8.12 at baseline to 4.01 at the end of treatment, in glycolic acid group the score decreased from 8.25 at baseline to 3.97 at week-10. During 10 weeks treatment mean of MASI score were similar in both groups and there were no statistical difference between groups (P > 0.05)

Garg et al Chandigarh [135] 2019	Group A treated with35% GA Group B treated with 35% GA+ 10%TCA combination Group C treated with 35% GA+ 20%TCA combination	30 Indian patients of melasma	Fortnightly superficial peel for 4 peels after priming for 2 weeks with 0.025% retinoic acid	Mean MASI at baseline was 14.330. In group A reduction in MASI reduced from 14.930 ± 9.260 to 7.650 ±5.975 after 4 peeling sessions. In group B MASI reduced from 14.040 ± 5.831 at baseline to 6.970 ± 2.980 after 4 peeling sessions .In group C MASI reduced from 14.020 ± 6.664 at baseline to 7.310 ± 4.781 after 4 peeling sessions. There was a con stant decrease in MASI scores after each peel as compared to the prepeel values (p < .00)

Grimes et al [14] has successfully demonstrated the efficacy and safety of 20% to 30% SA peels in melasma patients with skin types V and V1 whereas in another randomized control split face trial it was found to be ineffective in treatment of melasma.34

PHYTIC ACID COMBINATION PEEL :

Phytic acid has proven to be effective in the treatment of melasma and the typical burning sensation seen with glycolic acid is not observed with the phytic acid peels.[121]

Chemical peels can be associated with procedural side effects and complications, the most disturbing complication being Post inflammatory hyperpigmentation especially in dark skinned patients. The post peel pigmentation can be minimized with the help of adjunct topical agents known as priming agents which include 2-4% hydroquinone, 0.025% retinoic acid and 10% glycolic acid.

TABLE 3 Studies on priming agents along with chemical peels for melasma

Authors	Ethnicity	Priming agent	Peel	Response
Nanda et al. 2004.[136] Garg et al, 2008. [135]	50 Indian patients, 2 groups 60 Indian patients, 3 Groups	Group1:2% hydroquinone Group 11: 0.025% tretinoin Group I : none Group II : 0.025% tretinoin Group III : 2% hydroquinone	10-30% TCA Serial glycolic acid peels	More improvement with Hydroquinone in maintaining results and in decreasing PIH Results were better in group primed with hydroquinone compared to tretinoin and also decreasing PIH

Sarkar et al. [16] compared the therapeutic efficacy and tolerance of 35% glycolic acid (GA) (group A) to salicylic acid in combination with mandelic acid (20% salicylic acid and 10% mandelic acid) (group B) and to phytic acid (group C) in Indian melasma patients. Each group was prepared for 4 weeks before the procedure with 4% HQ and0.05% tretinoin. The chemical peel was performed every 14 days until the 12th week of the study. Improvement

was seen in all 3 groups, but was statistically significant in group A compared to group C, and in group B compared to group C, but there was no statistically significant difference between groups A and B.

Sahu et al. [137] examined the differences in the effectiveness of peelings using 15%TCA, 30% GA and 92% lactic acid. They showed that 15% of TCA is as effective as 30% of GA, while both exceeded the effectiveness of 92% of lactic acid. However, GA was better tolerated by the patients; therefore, according to the researchers, any of these peels can be used in clinical practice after taking into account the patient's profile. The authors suggest that the 30% GA peel is the best of the three peels; however, for aging, thin and sensitive skin, lactic acid may be preferred.

MATERIALS AND METHODS

PLACE OF STUDY: Department of Dermatology, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh.

DURATION OF STUDY: 1 year

STUDY DESIGN– Comparative interventional study.

SAMPLE SIZE: 96 patients of melasma from outpatient department of Santosh medical college.

ETHICAL CLEARENCE : Clearence from institutional ethical committee of Santosh medical college & Hospital Ghaziabad was obtained prior to conducting this study.

INCLUSION CRITERIA:

All clinically diagnosed fresh cases of melasma of either sex of ≥ 18 years

EXCLUSION CRITERIA : Pregnant or lactating women, Patient on any therapy for melasma for the past one month, Patient with tendencies of keloid formation, Patient with history of herpes labialis, Recently on oral contraceptives, Patient with unrealistic expectations

METHODOLOGY :

All clinically diagnosed fresh cases of melasma of either sex of ≥ 18 years who were willing to undergo the procedure of chemical peels and who gave a written consent were enrolled from the outpatient department of Santosh medical college & hospital, Ghaziabad and were randomly divided into 3 groups consisting of 32 patient each group. History was taken from each patient and demographic details like age, sex, residence, occupation, marital status was recorded. Further presenting complaint, site of onset, duration, progression, distribution, any previous topical therapy and it's duration, oral contraceptive pill (OCP) intake, family history, history of sun exposure, photosensitivity, history of any systemic illness & history relevant to exclusion criteria was taken and was noted. General physical, systemic and cutaneous examination for melasma was done, this

included the site, size & appearence of macules. Further photography was done at the time of enrolment, pre peel procedure on every sitting and on monthly basis during the three month follow up period. Patients were classified into epidermal, dermal, mixed type based on the depth of lesions with the help of dermoscope (dark brown with well defined network seen in epidermal melasma, shades of light brown with an irregular network is seen when located in lower epidermis whereas blue or bluish grey colour when dermal) and mixed type (showing features of both epidermal and dermal pattern). Further classification of melasma based on site as centrofacial, malar and mandibular type was done.

PROCEDURE FOR MODIFIED MASI SCORE :

Modified MASI score was done at the time of enrolment, pre peel procedure on every sitting and on monthly basis during the three month follow up period. Four areas of face were evaluated : 1. Forehead (F), 2. Right malar region (MR), 3. left malar region (ML), and 4. Chin (C), corresponding to 30%, 30%, 30%, 10% of the face resp. The area of involvement in each of these 4 areas was given numeric value of 0 to 6 (0 = no involvement;1 = 60%). Group A was treated with Glycolic acid(35%)(timpac company), group B was be treated with Salicylic(20%)-Mandelic(10%) peel (SM peel)(timpac company) and group C was treated with Phytic acid combination chemical peel(timpac company).

SKIN PRIMING:

All the patients were primed with 4% Hydroquinone, once daily at night for 4 weeks before starting chemical peels

PROCEDURE FOR CHEMICAL PEEL : Patient were asked to wash the face with soap and water to remove dirt. Patient were asked to pull the hair back using headband. Sensitive areas of the face like inner canthus of eyes and nasolabial folds were protected using vaseline The face was cleaned by scrubbing with a 2X2 inch cotton gauze piece soaked with methyl alcohol. In all patients the post auricular test peel was carried out to find any hypersensitivity to any ingredients of the peel. The peeling agent was then applied using a cotton tipped applicator, it was applied beginning from forehead, then the right cheek, nose, left cheek and chin in that order. Feathering strokes were applied at the edges to prevent demarcation lines. After completion time the patient was asked to wash with cold water. The face was then patted dry and rubbing had to be avoided. All the patients were advised total sun protection with a broad spectrum sunscreen at 2 hour intervals during daytime during the whole period of study. Patient were advised to use a mild cleanser. A total number of 6 sessions were done for each patient at 0, 2, 4 , 6, 8, 10 weeks .

Follow up: Patients were followed up monthly for three months to assess the response of treatment and to observe the side effects.

STATISTICAL ANALYSIS : A P value of <0.05 was considered to indicate statistical significance. The normality of quantitative data was checked by measures of Kolmogorov-Smirnov test of normality. For normally distributed data mean values of three groups was compared using one way analysis of variance (ANOVA). Analysis will be conducted using R software version 4.0.2

Observations and Results

All clinically diagnosed fresh cases of melasma of either sex of ≥ 18 years who agreed to undergo the procedure of chemical peels and and who had given written consent were enrolled from the outpatient department of Santosh medical college & hospital, Ghaziabad and they were randomly divided into 3 groups consisting of 32 patient each group. History were taken from each patient and demographic details like age, sex, residence, occupation, marital status were recorded. Further presenting complaint, site of onset, duration, progression, distribution, any previous topical therapy and it's duration, oral contraceptive pill (OCP) intake, family history, history of sun exposure, photosensitivity, history of any systemic illness & history relevant to exclusion criteria were taken and noted. General physical, systemic and cutaneous examination for melasma were done, this included the site, size & appearence of macules. Further photography was done at the time of enrolment, pre peel procedure on every sitting and on monthly basis during the three month follow up period. Patients were classified into epidermal, dermal, mixed type based on the depth of lesions with the help of dermoscope (dark brown with well defined network seen in epidermal melasma, shades of light brown with an irregular network is seen when located in lower epidermis whereas blue or bluish grey colour when dermal) and mixed type (showing features of both epidermal and dermal pattern).

Table 1: Distribution of the Melasma patients as per the age

	N	Minimum	Maximum	Mean	Std. Deviation
Age of the Patient	96	20	48	30.55	5.96

The mean age of all the Melasma patient in study is 30.55 ±5.96 years.

Table 2: Distribution of the Melasma patients as per the treatment types

Treatment Type	Frequency	Percent
Glycolic acid	32	33.3
Salicylic-Mandelic acid	32	33.3
Phytic acid combination	32	33.3
Total	96	100

Thirty two patients (33.3%) were allocated to all three groups.

Table 3: Distribution of the Melasma patients as per the Gender

Gender of the Patient	Frequency	Percent
Male	15	15.6
Female	81	84.4
Total	96	100.0

Majority of the patients i.e. 81(84.4%) were females out of total 96 patients.

Table 4: Distribution of the Melasma patients as per the Marital Status

Marital Status	Frequency	Percent
Married	93	96.9
Unmarried	3	3.1
Total	96	100.0

Majority of the patients i.e. 93(96.9%) were married out of total 96 patients.

Table 5: Distribution of the Melasma patients as per the Occupation

Occupation	Frequency	Percent
Clerck	2	2.1
Engineer	1	1.0
Farmer	26	27.1
Housewife	31	32.3
Nurse	2	2.1
Student	5	5.2
Teacher	9	9.4
Total	96	100.0

Majority of the patients i.e. 31(32.3%) were housewives followed by 26(27.1%) farmers. Minimum one patient was found to be engineer.

Table 6: Distribution of the Melasma patients as per the Clinical Type of Melasma

Clinical Type of Melasma	Frequency	Percent
Centrofacial	61	63.5
Malar	29	30.2
Mandibular	4	4.2
Not documented	2	2.1
Total	96	100.0

Majority of the patients i.e. 61(63.5%) had centrofacial type of Melasma as per clinical typing followed by Malar type of

Melasma in 29(30.21%) patients. Mandibular type was found only in 4(4.2%) patients.

Table 7: Distribution of the Melasma patients as per the Melasma Morphological Type

Morphological Type of Melasma	Frequency	Percent
Dermal	59	61.5
Epidermal	33	34.4
Not documented	4	4.2
Total	96	100.0

Majority of the patients i.e. 59(61.5%) had Dermal type of Melasma followed by Malar type of melasma in 33(34.4%) patients.

Mandibular type was found only in 4(4.2%) patients.

Table 8: Distribution of the Melasma patients as per the Fitzpatrick Skin Type in Melasma Patients

Fitzpatrick Skin Type	Frequency	Percent
Type III	7	7.3
Type IV	26	27.1
Type V	62	64.6
Not documented	1	1.0
Total	96	100.0

Majority of the patients i.e. 62(64.6%) belong to type V of Fitzpatrick Skin Type followed by type IV of Fitzpatrick Skin Type

of melasma in 26(27.1%) patients. Type IV of Fitzpatrick Skin Type was found only in 7(7.3%) patients.

Table 9: Distribution of the Melasma patients as per the Side Effects

Side Effects	Frequency	Percent
Burning Sensation	2	2.1
Erythema	7	7.3
No side effects	82	85.4
N/av	1	1.0
Post inflammatory hyperpigmentation	3	3.1
Rebound hyperpigmentation	1	1.0
Total	96	100.0

Majority of the patients i.e. 82(85.4%) had not felt any side effects. Erythema was observed in 7(7.3%) patients followed by

post inflammatory hyperpigmentation was felt in 3(3.1%) patients. Burning sensation was found in 2(2.1%) patients. Rebound

hypertension was found in 1(1%) of the patients. One patient did not

Table 10: Distribution of the Melasma patients as per the Physician Global Assessment Score

PHYSICIAN GLOBAL ASSESSMENT SCORE	Frequency	Percent
0	7	7.3
2	14	14.6
3	56	58.3
4	19	19.8
Total	96	100.0

On the evaluation of physician global assessment score, majority of the melasma patients i.e. 56(58.3%) patients has been found with PGA Score of 3 followed by 19(19.8%) patients with score of 4. Fourteen(14.6%) patients were found with physician global assessment score of 2. Minimum Seven(7.3%) patients were found with physician global assessment score of zero.

Table 11: Distribution of the Melasma patients as per the Patient global assessment score

Patient global assessment score	**Frequency**	**Percent**
0	7	7.3
1	2	2.1
2	16	16.7
3	64	66.7
4	6	6.2
5	1	1.0
Total	96	100.0

On the evaluation of patient global assessment score, majority of the melasma patients i.e. 64(66.7%) patients has been found with PGA Score of 3 followed by 16(16.7%) patients with score of 2. Seven(7.3%) patients were found with patient global assessment score of zero followed by 6(6.2%) patients with patient global assessment score of 4 followed by 2(2.1%) patients with global assessment score of one. Minimum one patient of patient global assessment score of 5.

Table 12: Distribution of the Melasma patients: Gender of the Patient Versus Treatment Type

Gender of the Patient	Statistics	Treatment Type		
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid combination
Male	Count	6	5	4
	% within Treatment Type	18.8%	15.6%	12.5%
Female	Count	26	27	28
	% within Treatment Type	81.2%	84.4%	87.5%
Total	Count	32	32	32
	% within Treatment Type	100.0%	100.0%	100.0%

Chi Square =0. .474, P value=0.789(Non significant)

Females were found to be more than three fourth in all the three groups.

Figure 1: Parallel bar chart depicting Distribution of the Melasma patients: Gender of the Patient Versus Treatment Type

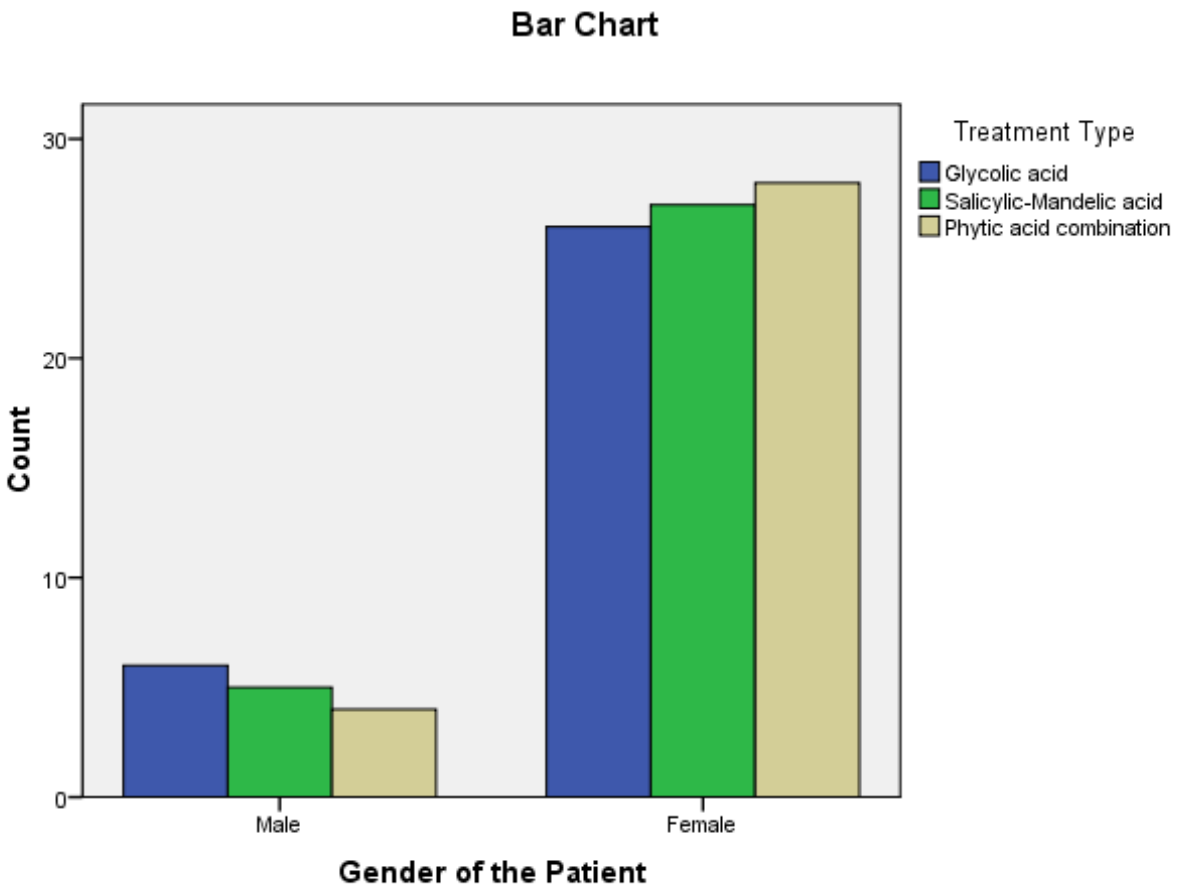


Table 13: Distribution of the Melasma patients: Marital Status Versus Treatment Type

Marital Status	Statistics	Treatment Type		
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid combination
Married	Count	32	32	29
	% within Treatment Type	100.0%	100.0%	90.6%
Unmarried	Count	0	0	3
	% within Treatment Type	.0%	.0%	9.4%
Total	Count	32	32	32
	% within Treatment Type	100.0%	100.0%	100.0%

Chi Square =6 .194, P value<0.05(Significant)

Only 3 (9.4%) patients of phytic acid group was unmarried, rest all of the patients were married.

Figure 2: Parallel bar chart depicting Distribution of the Melasma patients: Marital Status Versus Treatment Type

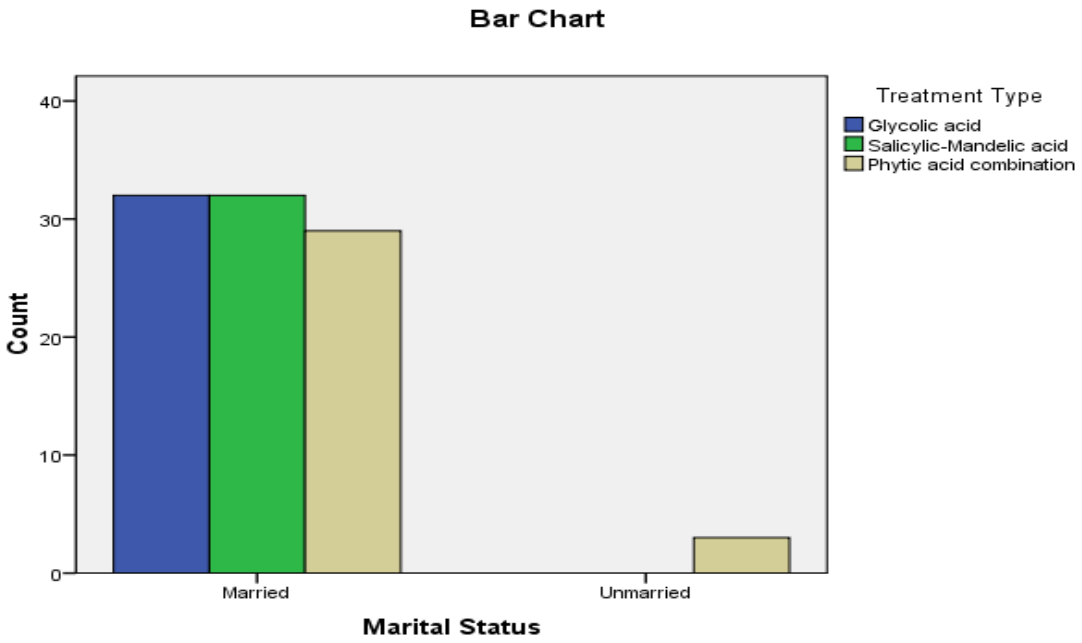


Table 14: Distribution of the Melasma patients: Occupation Versus Treatment Type

Occupation	Statistics	Treatment Type			Total
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid combination	
Engineer	Count	1	0	0	1
	% within Treatment Type	3.1%	.0%	.0%	1.0%
Clerk	Count	0	1	1	2
	% within Treatment Type	.0%	3.1%	3.1%	2.1%
Farmer	Count	9	10	7	26
	% within Treatment Type	28.1%	31.2%	21.9%	27.1%
Housewife	Count	19	0	12	31
	% within Treatment Type	59.4%	.0%	37.5%	32.3%
Nurse	Count	0	2	0	2
	% within Treatment Type	.0%	6.2%	.0%	2.1%
Student	Count	0	3	2	5
	% within Treatment Type	.0%	9.4%	6.2%	5.2%
Teacher	Count	3	3	3	9
	% within Treatment Type	9.4%	9.4%	9.4%	9.4%
Total	Count	32	32	32	96
	% within Treatment Type	100.0%	100.0%	100.0%	100.0%

Chi Square =40.94, P value<0.05(Significant)

In glycolic acid as well as phytic acid combinations, majority of the patients were found to be housewives. Among SMA group, majority were found to be farmers and this distribution was found statistically statistically significant,

Figure 3: Parallel bar chart depicting Distribution of the Melasma patients: Occupation Versus Treatment Type

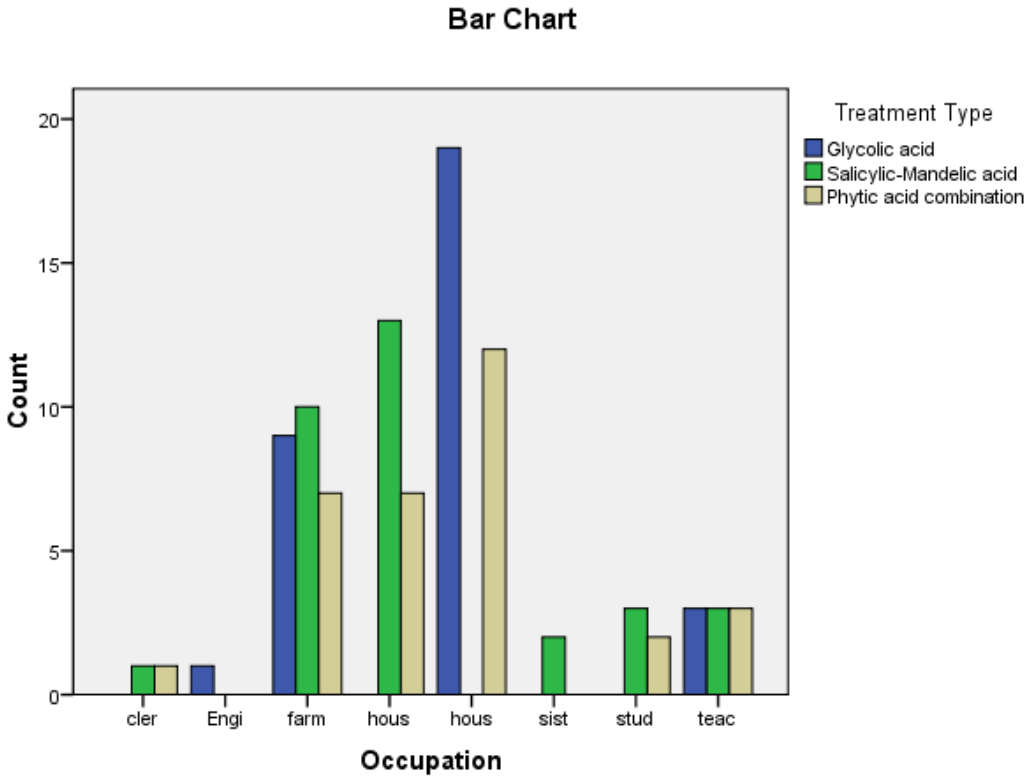


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Table 15: Distribution of the Melasma patients: Melasma Clinical Type Versus Treatment Type

Melasma Clinical Type	Statistics	Treatment Type			Total
		Glycolic acid	Salicylic-Mandelic	Phytic acid combination	
Not Documented	Count	0	1	1	2
	% within Treatment Type	.0%	3.1%	3.1%	2.1%
Centrofacial	Count	22	19	20	61
	% within Treatment Type	68.8%	59.4%	62.5%	63.5%
Malar	Count	9	10	10	29
	% within Treatment Type	28.1%	31.2%	31.2%	30.2%
Mandibular	Count	1	2	1	4
	% within Treatment Type	3.1%	6.2%	3.1%	4.2%
Total	Count	32	32	32	96
	% within Treatment Type	100.0%	100.0%	100.0%	100.0%

Chi Square =1.798, P value=0.937(Non significant)

In more than half of the cases, Centrofacial type was found dominantly in all the three treatment groups and this distribution was found statistically non significant.

Figure 4: Parallel bar chart depicting Distribution of the Melasma patients: Clinical Type Versus Treatment Type

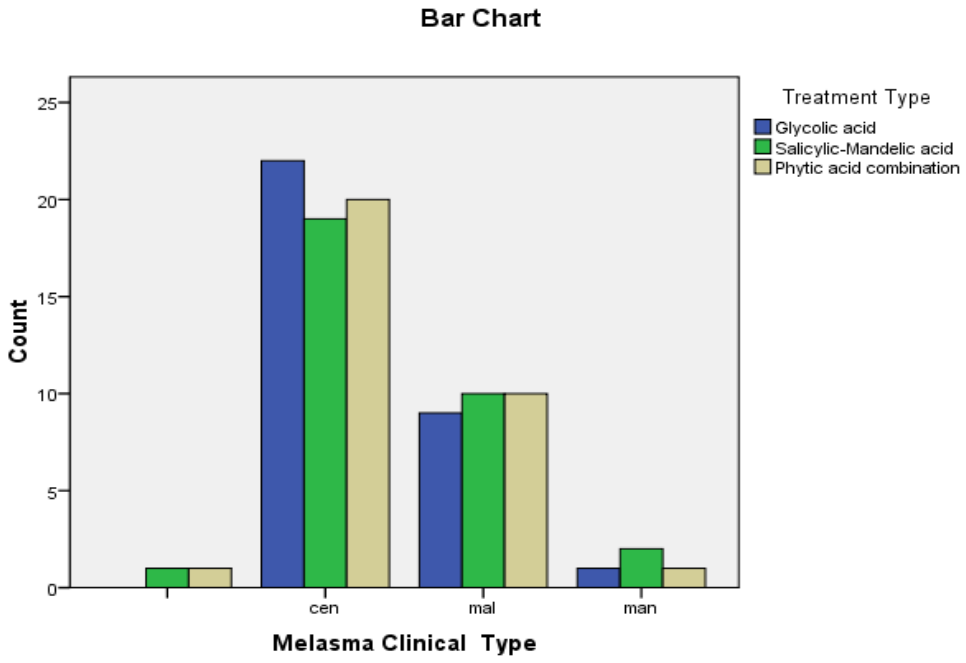

Table 16: Distribution of the Melasma patients: Melasma Morphological Type Versus Treatment Type

Melasma Morphological Type	Statistics	Treatment Type			Total
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid	
Mixed	Count	0	3	1	4
	% within Treatment Type	.0%	9.4%	3.1%	4.2%
Dermal	Count	20	19	20	59
	% within Treatment Type	62.5%	59.4%	62.5%	61.5%
Epidermal	Count	1	10	11	33
	% within Treatment Type	37.5%	31.2%	34.4%	34.4%
Total	Count	32	32	32	96
	% within Treatment Type	100.0%	100.0%	100.0%	100.0%

Chi Square = 3.716, P value=0.446(Non significant)

Dermal morphological type of melasma was found in more than half of the cases in all three treatment group and this distribution was found statistically non significant,

Figure 5: Parallel bar chart depicting Distribution of the Melasma patients: Morphological Type Versus Treatment Type

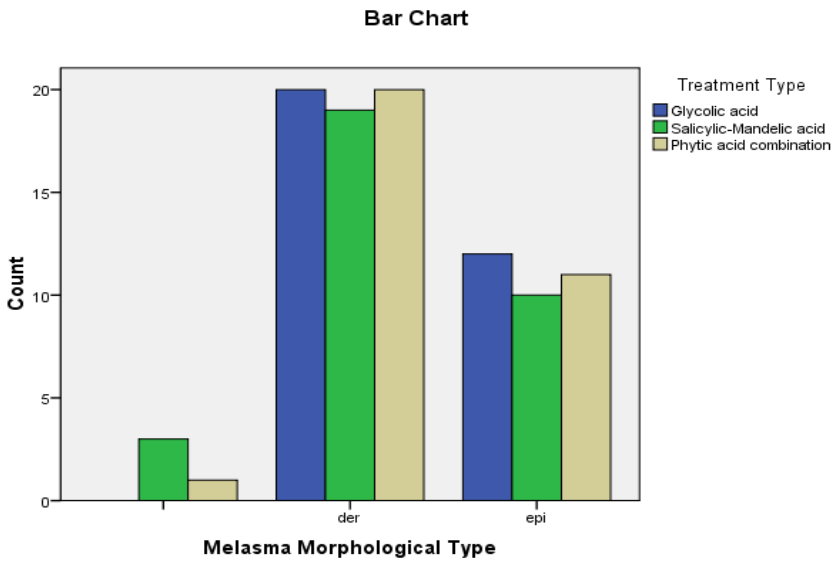

Table 17: Distribution of the Melasma patients: Fitzpatrick Skin Type Versus Treatment Type

Fitzpatrick Skin Type	Statistics	Treatment Type			Total
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid combination	
III	Count	2	2	3	7
	% within Treatment Type	6.2%	6.2%	9.4%	7.3%
IV	Count	8	8	10	26
	% within Treatment Type	25.0%	25.0%	31.2%	27.1%
V	Count	22	21	19	62
	% within Treatment Type	68.8%	65.6%	59.4%	64.6%
Not reported	Count	0	1	0	1
	% within Treatment Type	.0%	3.1%	.0%	1.0%
Total	Count	32	32	32	96
	% within Treatment Type	100.0%	100.0%	100.0%	100.0%

Chi Square =2 .819, P value=0.831(Non significant)

Majority of the patients in all the three treatment groups were found with Fitzpatrick Skin Type V and this distribution was found statistically non significant.

Figure 6: Parallel bar chart depicting Distribution of the Melasma patients: Occupation Versus Treatment Type

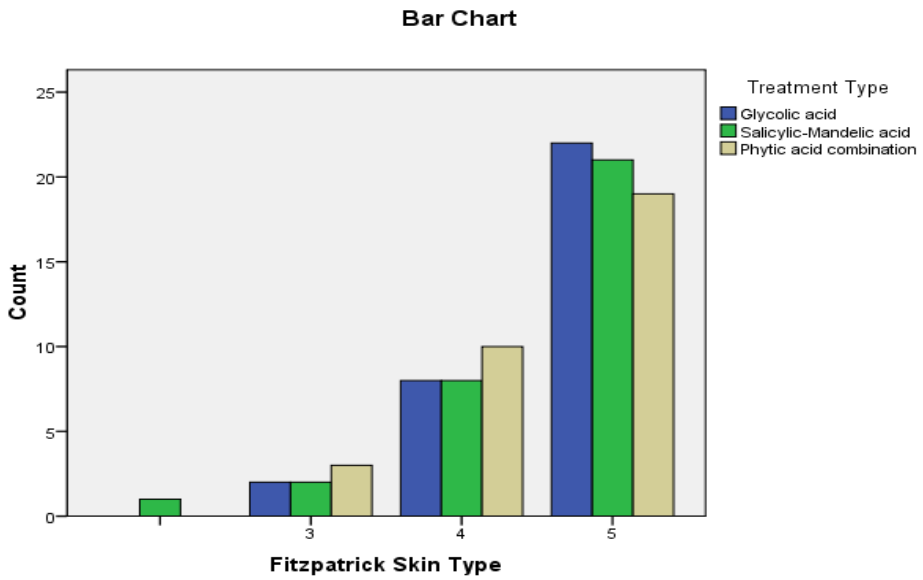

Table 18: Distribution of the Melasma patients: Side Effects Versus Treatment Type

Side Effects	Statistics	Treatment Type			Total
		Glycolic acid	Salicylic-Mandelic acid	Phytic acid	
Not Available	Count	1	0	0	1
	% within Treatment Type	3.1%	.0%	.0%	1.0%
Post inflammatory	Count	2	1	0	3
	% within Treatment Type	6.2%	3.1%	.0%	3.1%
Burning Sensation	Count	2	0	0	2
	% within Treatment Type	6.2%	.0%	.0%	2.1%
Erythema	Count	5	1	1	7
	% within Treatment Type	15.6%	3.1%	3.1%	7.3%
No Side Effects	Count	22	29	31	82
	% within Treatment Type	68.8%	90.6%	96.9%	85.4%
Rebound Hyperpigmentation	Count	0	1	0	1
	% within Treatment Type	.0%	3.1%	.0%	1.0%
Total	Count	32	32	32	96
	% within Treatment Type	100.0%	100.0%	100.0%	100.0%

Chi square =16.20, P value<0.05(Significant)

Majority of the patients in all the treatment groups did observe any side effects. Erythema was found in 5 patients in glycolic acid group. This distribution was found statistically significant(p value<0.05)

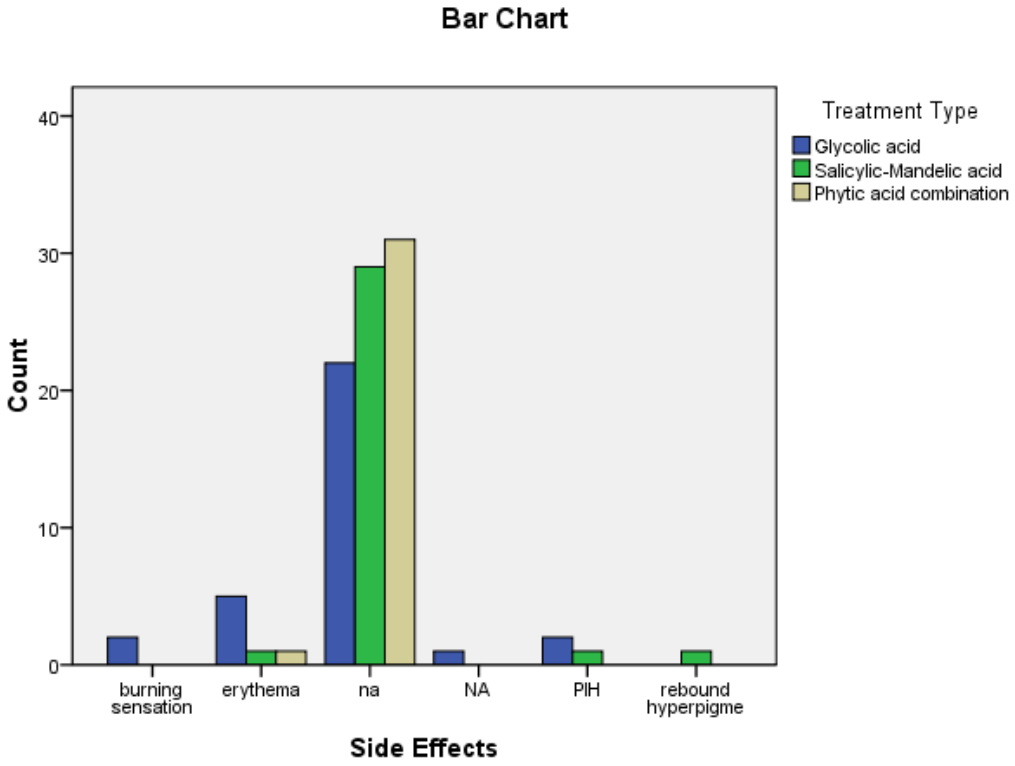

Table 19: Mean Value of Visual Analogue Scale Score Scores of All Melasma Patients at Various Time Points

The mean value of VAS at enrolment was found. The Mean Visual Analogue Scale Score 2 Weeks is found to be 2.32± 0.75. It was further improved to 2.58 ± 0.72 at 4 weeks. The Mean Visual Analogue Scale Score Weeks is found to be 2.58± 0.75 at . It was further improved to 2.98 ± 0.89 at 6 weeks. VAS Score has further improved to 3.28 ± 1.05 at 8 weeks. The mean VAS Score at 10 weeks was found to be 3.10 ±1.09. The Mean Visual Analogue Scale Score 14 Weeks is found to be 3.09± 0.9. It was decreased to 2.78 ± 0.72 at 18 weeks. The mean VAS score has finally reached to 2.56± 1.09.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Visual Analogue Scale Score At Enrolment	96	1	1	1.00	.000
Visual Analogue Scale Score 2 Weeks	96	1	5	2.32	.747
Visual Analogue Scale Score 4 Weeks	96	1	4	2.58	.721
Visual Analogue Scale Score 6 Weeks	96	1	5	2.98	.894
Visual Analogue Scale Score 8 Weeks	96	1	5	3.28	1.053
Visual Analogue Scale Score 10 Weeks	96	1	5	3.10	1.090
Visual Analogue Scale Score 14 Weeks	96	1	5	3.09	.919
Visual Analogue Scale Score 18 Weeks	96	1	5	2.78	1.028
Visual Analogue Scale Score 22 Weeks	96	1	4	2.56	1.094

Table 20: Mean value of MASI Scores of all Melasma patients at various time points

Variables	N	Minimum	Maximum	Mean	Std. Deviation
MASI 2 Weeks	96	3	25	14.90	5.353
MASI 4 Weeks	96	2.8	25	15.47	4.910
MASI 6 Weeks	96	2.8	22.8	13.20	4.761
MASI 8 Weeks	96	2	22	11.41	4.448
MASI 10 Weeks	96	2	21.6	10.83	4.287
MASI 14 Weeks	96	1.8	21.6	10.04	4.171
MASI 18 Weeks	94	1.8	21.6	10.24	4.250
MASI 22 Weeks	96	1.8	21.6	10.35	4.423

Table 21: Mean value of Patient improvement as well as assessment scales of all Melasma patients at various time points

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Percentage Reduction at 14th week	96	8	90	45.82	17.251
Percentage Reduction at 22nd week	96	8	92	43.55	17.283
Phy GA	96	0	4	2.83	.991
Patients GA	96	0	5	2.66	.950

Table 22: Mean value of Age of among all three groups of Melasma patients at various time points

Variable	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
Age of the Melasma Patient	Glycolic acid	32	31.28	6.36	1.125	0.681
	Salicylic-Mandelic acid	32	30.38	5.22	.922	
	Phytic acid combination	32	30.00	6.34	1.120	

The mean age of Melasma patients in Glycolic acid treatment group is 31.28 ±6.36 years whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 30.38 ±5.22. The mean age of the melasma patietns in Phytic Acid combination is 30.00 ±6.34. This distribution of age among various treatment group of patients was found to be statistically non significant(p value<0.05).

Table 23: Mean Value of Visual Analogue Scale Score Scores of Melasma Patients at Various Time Points among three treatment groups

Variables	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
Visual Analogue Scale Score at Enrolment	Glycolic acid	32	1.00	.000[a]	.000	
	Salicylic-Mandelic acid	32	1.00	.000[a]	.000	
	Phytic acid combination	32	1.00	.000[a]	.000	

Table 24: Mean Value of Visual Analogue Scale Score Scores of Melasma Patients at Various Time Points among three treatment groups

Variables	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
Visual Analogue Scale Score 2 Weeks	Glycolic acid	32	2.03	.740	.131	.003
	Salicylic-Mandelic acid	32	2.66	.865	.153	
	Phytic acid combination	32	2.28	.457	.081	

Table 25: Mean Value of Visual Analogue Scale Score Scores of Melasma Patients at Various Time Points among three treatment groups

Variables	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
Visual Analogue Scale Score 4 Weeks	Glycolic acid	32	2.50	.568	.100	.014
	Salicylic-Mandelic acid	32	2.88	.751	.133	
	Phytic acid combination	32	2.38	.751	.133	

Table 26: Mean Value of Visual Analogue Scale Score Scores of Melasma Patients at Various Time Points among three treatment groups

Variables	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
Visual Analogue Scale Score 4 Weeks	Glycolic acid	32	2.50	.568	.100	.014
	Salicylic-Mandelic acid	32	2.88	.751	.133	
	Phytic acid combination	32	2.38	.751	.133	
Visual Analogue Scale Score 6 Weeks	Glycolic acid	32	3.03	.861	.152	.004
	Salicylic-Mandelic acid	32	3.31	.896	.158	
	Phytic acid combination	32	2.59	.798	.141	
Visual Analogue Scale Score 8 Weeks	Glycolic acid	32	3.69	.693	.122	.000
	Salicylic-Mandelic acid	32	3.50	1.016	.180	
	Phytic acid combination	32	2.66	1.125	.199	
Visual Analogue Scale Score 10 Weeks	Glycolic acid	32	3.84	.884	.156	.000
	Salicylic-Mandelic acid	32	3.28	.888	.157	
	Phytic acid combination	32	2.19	.780	.138	
Visual Analogue Scale Score 14 Weeks	Glycolic acid	32	3.81	.592	.105	.000
	Salicylic-Mandelic acid	32	3.06	.914	.162	
	Phytic acid combination	32	2.41	.615	.109	
Visual Analogue Scale Score 18 Weeks	Glycolic acid	32	3.59	.499	.088	.000
	Salicylic-Mandelic acid	32	2.69	1.030	.182	
	Phytic acid combination	32	2.06	.840	.148	
Visual Analogue Scale Score 22 Weeks	Glycolic acid	32	3.62	.492	.087	.000
	Salicylic-Mandelic acid	32	2.31	1.030	.182	
	Phytic acid combination	32	1.75	.672	.119	

Table 27: Mean Value of MASI Scores of Melasma Patients At Enrolment between GA & SMA Group treatment groups

					Std. Error	P value
MASI at Enrolment	Glycolic acid	32	16.456	5.5334	.9782	0.897
	Salicylic-Mandelic acid	32	16.635	5.4771	.9682	

Table 28: Mean Value of MASI Scores of Melasma Patients At Enrolment between SMA & PA Group treatment groups

					Std. Error	P value
MASI at Enrolment	Salicylic-Mandelic acid	32	16.635	5.4771	.9682	0.139
	Phytic acid combination	32	14.597	5.3992	.9545	

Table 29: Mean Value of MASI Scores of Melasma Patients At Enrolment between GA & PA Group treatment groups

					Std. Error	P value
MASI at Enrolment	Glycolic acid	32	16.456	5.5334	.9782	0.179
	Phytic acid combination	32	14.597	5.3992	.9545	

Table 30: Mean Value of MASI Scores of Melasma Patients At Enrolment among three treatment groups

Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value between GA & SMA Group	P Value between SMA & PA Group	P Value between GA & PA Group	P value Among All three groups
Glycolic acid	32	16.46	5.53	0.98	0.897	0.139	0.179	0.261
Salicylic-Mandelic acid	32	16.64	5.48	0.97				
Phytic acid combination	32	14.60	5.40	0.95				

The mean Value of MASI Scores of Melasma patients at enrolment in Glycolic acid treatment group is 16.46 ± 5.53 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 16.64 ± 5.48. The mean Value of MASI Scores of the melasma patients at enrolment in Phytic Acid combination is 16.64 ± 5.48. This distribution of mean MASI score among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA

MASI at Enrolment					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	81.568	2	40.784	1.363	.261
Within Groups	2782.841	93	29.923		
Total	2864.409	95			

MASI Scores at 2 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 2 Weeks	Glycolic acid	32	15.813	5.5689	.9844	0.657
	Salicylic-Mandelic acid	32	15.225	4.9351	.8724	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P value
MASI 2 Weeks	Salicylic-Mandelic acid	32	15.225	4.9351	.8724	0.332
	Phytic acid combination	32	13.963	5.3830	.9516	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 2 Weeks	Glycolic acid	32	15.813	5.5689	.9844	0.182
	Phytic acid combination	32	13.963	5.3830	.9516	

Table: Mean Value of MASI Score Scores of Melasma Patients at 2 weeks among three treatment groups

Treatment Type	N	Mean	Std. Deviation	Std Error Mean	P Value between GA & SMA Group	P Value between SMA & PA Group	P Value between GA & PA Group	P value Among All three groups
Glycolic acid	32	15.81	5.57	0.98	0.657		0.182	0.366
Salicylic-Mandelic acid	32	15.23	4.94	0.87		0.332		
Phytic acid combination	32	13.96	5.38	0.95				

The mean Value of MASI Scores of Melasma patients at 2 Weeks in Glycolic acid treatment group is 15.81 ± 5.57 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 15.23 ± 4.94. The mean Value of MASI Scores of the melasma patients at 2 weeks in Phytic Acid combination is 13.96 ± 5.38. This distribution of mean MASI score at 2 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 2 Weeks					
	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	57.190	2	28.595	1.017	0.366
Within Groups	2614.650	93	28.115		
Total	2671.840	95			

4 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 4 Weeks	Glycolic acid	32	15.091	5.3699	.9493	0.400
	Salicylic-Mandelic acid	32	14.063	4.2737	.7555	

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 4 Weeks	Salicylic-Mandelic acid	32	14.063	4.2737	.7555	0.414
	Phytic acid combination	32	17.878	25.8675	4.5728	

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 4 Weeks	Glycolic acid	32	15.091	5.3699	.9493	0.553
	Phytic acid combination	32	17.878	25.8675	4.5728	

Table: Mean Value of MASI Score Scores of Melasma Patients at 4 weeks among three treatment groups

Treatment Type	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P Value between GA & SMA Group**	**P Value between SMA & PA Group**	**P Value between GA & PA Group**	**P value Among All three groups**
Glycolic acid	32	15.09	5.37	.9493	0.400		0.553	0.210
Salicylic-Mandelic acid	32	14.06	4.27	.7555		0.414		
Phytic acid combination	32	13.62	25.87	4.5728				

The mean Value of MASI Scores of Melasma patients at 4 Weeks in Glycolic acid treatment group is 15.09 ± 5.37 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 14.06 ± 4.27. The mean Value of MASI Scores of the melasma patients at 4 weeks in Phytic Acid combination is 13.62 ± 25.87. This distribution of mean MASI score at 4 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 4 Weeks					
	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	249.453	2	124.726	.522	.595
Within Groups	22203.017	93	238.742		
Total	22452.470	95			

6 Weeks

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 6 Weeks	Salicylic-Mandelic acid	32	12.833	3.6542	.6460	0.723
	Phytic acid combination	32	13.226	5.0354	.8901	

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P value
MASI 6 Weeks	Glycolic acid	32	14.309	5.4872	.9700	0.414
	Phytic acid combination	32	13.226	5.0354	.8901	

Table: Mean Value of MASI Score Scores of Melasma Patients at 6 weeks among three treatment groups

Treatment Type	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P Value between GA & SMA Group**	**P Value between SMA & PA Group**	**P Value between GA & PA Group**	**P value Among All three groups**
Glycolic acid	32	14.31	5.49	.9700	0.210		0.414	0.446
Salicylic-Mandelic acid	32	12.83	3.65	.6460		0.723		
Phytic acid combination	32	13.23	5.04	.8901				

The mean Value of MASI Scores of Melasma patients at 6 Weeks in Glycolic acid treatment group is 14.31 ± 5.49 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 12.83 ± 3.65. The mean Value of MASI Scores of the melasma patients at 6 weeks in Phytic Acid combination is 13.23 ± 5.04. This distribution of mean MASI score at 6 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 6 Weeks					
	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	37.405	2	18.702	.815	0.446
Within Groups	2133.345	93	22.939		
Total	2170.750	95			

8 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 8 Weeks	Glycolic acid	32	12.391	4.8233	.8526	0.357
	Salicylic-Mandelic acid	32	11.391	3.7312	.6596	

	Treatment Type	N	Mean	Std.	Std. Error Mean	P Value
MASI 8 Weeks	Salicylic-Mandelic acid	32	11.391	3.7312	.6596	0.312
	Phytic acid combination	32	12.531	5.1197	.9050	

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 8 Weeks	Glycolic acid	32	12.391	4.8233	.8526	0.910
	Phytic acid combination	32	12.531	5.1197	.9050	

Table : Mean Value of MASI Score Scores of Melasma Patients At 8 Weeks among three treatment groups

Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value between GA & SMA Group	P Value between SMA & PA Group	P Value between GA & PA Group	P value Among All three groups
Glycolic acid	32	12.39	4.82	.8526	0.357	0.312	0.910	0.559
Salicylic-Mandelic acid	32	11.39	3.73	.6596				
Phytic acid combination	32	12.53	5.12	.9050				

The mean Value of MASI Scores of Melasma patients at 8 Weeks in Glycolic acid treatment group is 12.39 ± 4.82 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 11.39 ± 3.73. The mean Value of MASI Scores of the melasma patients at 8 weeks in Phytic Acid combination is 12.53 ± 5.12. This distribution of mean MASI score at 8 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 8 Weeks					
	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	24.755	2	12.378	.586	.559
Within Groups	1965.303	93	21.132		
Total	1990.058	95			

10 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P
MASI 10 Weeks	Glycolic acid	32	11.403	4.5196	.7990	0.881
	Salicylic-Mandelic Acid	32	11.247	3.7475	.6625	

Group Statistics						
	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P value
MASI 10 Weeks	Salicylic-Mandelic acid	32	11.247	3.7475	.6625	0.487
	Phytic acid combination	32	12.026	5.0705	.8963	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 10 Weeks	Glycolic acid	32	11.403	4.5196	.7990	0.606
	Phytic acid combination	32	12.026	5.0705	.8963	

Table: Mean Value of MASI Score Scores of Melasma Patients At 10 Weeks among three treatment groups

Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	**P Value between GA & SMA Group**	**P Value between SMA & PA**	**P Value between GA & PA Group**	**P value Among All three groups**
Glycolic acid	32	11.40	4.52	.7990	0.881		0.606	0.763
Salicylic-Mandelic acid	32	11.25	3.75	.6625		0.487		
Phytic acid combination	32	12.03	5.07	.8963				

The mean Value of MASI Scores of Melasma patients at 10 Weeks in Glycolic acid treatment group is 11.40 ± 4.52 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 11.25 ± 3.75. The mean Value of MASI Scores of the melasma patients at 10 weeks in Phytic Acid combination is 12.03 ± 5.07. This distribution of mean MASI score at 10 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 10 Weeks					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	10.881	2	5.441	.271	0.763
Within Groups	1865.597	93	20.060		
Total	1876.478	95			

14 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 14 Weeks	Glycolic acid	32	10.230	4.3792	.7741	.607
	Salicylic-Mandelic acid	32	10.777	4.0787	.7210	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 14 Weeks	Salicylic-Mandelic acid	32	10.777	4.0787	.7210	0.441
	Phytic acid combination	32	11.657	4.9620	.8772	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 14 Weeks	Glycolic acid	32	10.230	4.3792	.7741	0.227
	Phytic acid combination	32	11.657	4.9620	.8772	

Table: Mean Value of MASI Score Scores of Melasma Patients at 14 Weeks among three treatment groups

Treatment Type	**N**	**Mean**	**Std. Deviation**	**Std. Error**	**P Value between GA & SMA Group**	**P Value between SMA & PA Group**	**P Value between GA & PA Group**	**P value Among All**
Glycolic acid	32	10.23	4.38	.7741	0.607		0.227	0.442
Salicylic-Mandelic acid	32	10.77	4.08	.7210		0.441		
Phytic acid combination	32	11.66	4.96	.8772				

The mean Value of MASI Scores of Melasma patients at 14 Weeks in Glycolic acid reatment group is 10.23 ± 4.38 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 10.77 ± 4.08. The mean Value of MASI Scores of the melasma patients at 14 weeks in Phytic Acid combination is 11.66 ± 4.96. This distribution of mean MASI score at 14 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 14 Weeks					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	33.154	2	16.577	.823	.442
Within Groups	1873.494	93	20.145		
Total	1906.649	95			

18 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 18 Weeks	Glycolic acid	31	10.032	4.3017	.7726	0.147
	Salicylic-Mandelic acid	32	11.632	4.3538	.7697	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 18 Weeks	Salicylic-Mandelic acid	32	11.632	4.3538	.7697	0.880
	Phytic acid combination	32	11.810	5.0049	.8847	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 18 Weeks	Glycolic acid	31	10.032	4.3017	.7726	0.136
	Phytic acid combination	32	11.810	5.0049	.8847	

Table: Mean Value of MASI Score Scores of Melasma Patients at 18 Weeks among three treatment groups

Treatment Type	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P Value between GA & SMA Group**	**P Value between SMA & PA Group**	**P Value between GA & PA Group**	**P value Among All three groups**
Glycolic acid	31	10.03	4.30	.7726	0.147		0.136	0.242
Salicylic-Mandelic acid	32	11.63	4.35	.7697		0.880		
Phytic acid combination	32	11.81	5.00	.8847				

The mean Value of MASI Scores of Melasma patients at 18 Weeks in Glycolic acid treatment group is 10.03 ± 4.30 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 11.63 ± 4.35. The mean Value of MASI Scores of the melasma patients at 18 weeks in Phytic Acid combination is 11.81 ± 5.00. This distribution of mean MASI score at 18 weeks among various treatment group of patients between each two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 18 Weeks					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	60.107	2	30.054	1.441	.242
Within Groups	1919.286	92	20.862		
Total	1979.393	94			

22 Weeks

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 22 Weeks	Glycolic acid	32	9.81	4.1900	.7407	0.037
	Salicylic-Mandelic acid	32	12.24	4.8964	.8656	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P Value
MASI 22 Weeks	Salicylic-Mandelic acid	32	12.24	4.8964	.8656	0.577
	Phytic acid combination	32	11.55	4.9522	.8754	

	Treatment Type	N	Mean	Std. Deviation	Std. Error Mean	P value
MASI 22 Weeks	Glycolic acid	32	9.81	4.1900	.7407	0.135
	Phytic acid combination	32	11.55	4.9522	.8754	

Table: Mean Value of MASI Score Scores of Melasma Patients at 22 Weeks among three treatment groups

Treatment Type	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P Value between GA & SMA Group**	**P Value between SMA & PA Group**	**P Value between GA & PA Group**	**P value Among All three groups**
Glycolic acid	32	9.81	4.19	.7407	0.037		0.135	0.108
Salicylic-Mandelic acid	32	12.24	4.90	.8656		0.577		
Phytic acid combination	32	11.55	4.95	.8754				

The mean Value of MASI Scores of Melasma patients at 22 Weeks in Glycolic acid treatment group is 9.81 ± 4.19 whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 12.24 ± 4.90. The mean Value of MASI Scores of the melasma patients at 18 weeks in Phytic Acid combination is 11.55 ± 4.95. This distribution of mean MASI score at 18 weeks between GA & SMA Group was found statistically significant(p value<0.05). This distribution of mean MASI score at 18 weeks among various treatment group of patients between other two groups as well as among all groups was found to be statistically non significant.

ANOVA					
MASI 22 Weeks					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	100.289	2	50.144	2.277	0.108
Within Groups	2047.716	93	22.018		
Total	2148.005	95			

Table 24: Percentage reduction of Melasma at 14 and 22 weeks

	14 weeks	**22 weeks**
Glycolic acid	40.03	41.78
Salicylic mandelic acid	35.69	26.81
Phytic acid	22.00	23.20

GLYCOLIC ACID PATIENTS

Paired Samples Statistics					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS Enrolment	1.00	32	.000	.000
	VAS 8 Weeks	3.69	32	.693	.122
Pair 2	VAS Enrolment	1.00	32	.000	.000
	VAS 14 Weeks	3.81	32	.592	.105
Pair 3	VAS Enrolment	1.00	32	.000	.000
	VAS 22 Weeks	3.62	32	.492	.087
Pair 4	MASI at Enrolment	16.456	32	5.5334	.9782
	MASI 8 Weeks	12.391	32	4.8233	.8526
Pair 5	MASI at Enrolment	16.456	32	5.5334	.9782
	MASI 14 Weeks	10.230	32	4.3792	.7741
Pair 6	MASI at Enrolment	16.456	32	5.5334	.9782
	MASI 22 Weeks	9.808	32	4.1900	.7407

Paired Samples Correlations				
		N	Correlation	Sig.
Pair 1	VAS Enrolment & VAS 8 Weeks	32	.	.
Pair 2	VAS Enrolment & VAS 14 Weeks	32	.	.
Pair 3	VAS Enrolment & VAS 22 Weeks	32	.	.
Pair 4	MASI at Enrolment & MASI 8 Weeks	32	.891	.000
Pair 5	MASI at Enrolment & MASI 14 Weeks	32	.822	.000
Pair 6	MASI at Enrolment & MASI 22 Weeks	32	.792	.000

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	VAS Enrolment - VAS 8 Weeks	-2.688	.693	.122	-2.937	-2.438	-21.94	31	.000
Pair 2	VAS Enrolment - VAS 14 Weeks	-2.812	.592	.105	-3.026	-2.599	-26.86	31	.000
Pair 3	VAS Enrolment - VAS 22 Weeks	-2.625	.492	.087	-2.802	-2.448	-30.18	31	.000
Pair 4	MASI at Enrolment - MASI 8 Weeks	4.0656	2.5093	.4436	3.1609	4.9703	9.165	31	.000
Pair 5	MASI at Enrolment - MASI 14 Weeks	6.2259	3.1567	.5580	5.0878	7.3641	11.15	31	.000
Pair 6	MASI at Enrolment - MASI 22 Weeks	6.6478	3.3838	.5982	5.4278	7.8678	11.11	31	.000

SMA

Paired Samples Statistics					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS Enrolment	1.00	32	.000	.000
	VAS 8 Weeks	3.50	32	1.016	.180
Pair 2	VAS Enrolment	1.00	32	.000	.000
	VAS 14 Weeks	3.06	32	.914	.162
Pair 3	VAS Enrolment	1.00	32	.000	.000
	VAS 22 Weeks	2.31	32	1.030	.182
Pair 4	MASI at Enrolment	16.635	32	5.4771	.9682
	MASI 8 Weeks	11.391	32	3.7312	.6596
Pair 5	MASI at Enrolment	16.635	32	5.4771	.9682
	MASI 14 Weeks	10.777	32	4.0787	.7210
Pair 6	MASI at Enrolment	16.635	32	5.4771	.9682
	MASI 22 Weeks	12.238	32	4.8964	.8656

Paired Samples Correlations				
		N	Correlation	Sig.
Pair 1	VAS Enrolment & VAS 8 Weeks	32	.	.
Pair 2	VAS Enrolment & VAS 14 Weeks	32	.	.
Pair 3	VAS Enrolment & VAS 22 Weeks	32	.	.
Pair 4	MASI at Enrolment & MASI 8 Weeks	32	.830	.000
Pair 5	MASI at Enrolment & MASI 14 Weeks	32	.838	.000
Pair 6	MASI at Enrolment & MASI 22 Weeks	32	.710	.000

Paired Samples Test									
		Paired Differences							
					95% Confidence Interval of the Difference				
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)
Pair 1	VAS Enrolment - VAS 8 Weeks	-2.500	1.016	.180	-2.866	-2.134	-13.91	31	.000
Pair 2	VAS Enrolment - VAS 14 Weeks	-2.062	.914	.162	-2.392	-1.733	-12.77	31	.000
Pair 3	VAS Enrolment - VAS 22 Weeks	-1.312	1.030	.182	-1.684	-.941	-7.210	31	.000
Pair 4	MASI at Enrolment - MASI 8 Weeks	5.2447	3.1595	.5585	4.105	6.3838	9.390	31	.000
Pair 5	MASI at Enrolment - MASI 14 Weeks	5.8584	3.0313	.5359	4.765	6.9513	10.93	31	.000
Pair 6	MASI at Enrolment - MASI 22 Weeks	4.3975	3.9874	.7049	2.959	5.8351	6.239	31	.000

Phytic Acid Combination

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	VAS Enrolment	1.00	32	.000	.000
	VAS 8 Weeks	2.66	32	1.125	.199
Pair 2	VAS Enrolment	1.00	32	.000	.000
	VAS 14 Weeks	2.41	32	.615	.109
Pair 3	VAS Enrolment	1.00	32	.000	.000
	VAS 22 Weeks	1.75	32	.672	.119
Pair 4	MASI at Enrolment	14.597	32	5.3992	.9545
	MASI 8 Weeks	12.531	32	5.1197	.9050
Pair 5	MASI at Enrolment	14.597	32	5.3992	.9545
	MASI 14 Weeks	11.657	32	4.9620	.8772
Pair 6	MASI at Enrolment	14.597	32	5.3992	.9545
	MASI 22 Weeks	11.547	32	4.9522	.8754

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	VAS Enrolment & VAS 8 Weeks	32	.	.
Pair 2	VAS Enrolment & VAS 14 Weeks	32	.	.
Pair 3	VAS Enrolment & VAS 22 Weeks	32	.	.
Pair 4	MASI at Enrolment & MASI 8 Weeks	32	.960	.000
Pair 5	MASI at Enrolment & MASI 14 Weeks	32	.912	.000
Pair 6	MASI at Enrolment & MASI 22 Weeks	32	.984	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	VAS Enrolment - VAS 8 Weeks	-1.656	1.125	.199	-2.062	-1.251	-8.330	31	.000
Pair 2	VAS Enrolment - VAS 14 Weeks	-1.406	.615	.109	-1.628	-1.185	-12.93	31	.000
Pair 3	VAS Enrolment - VAS 22 Weeks	-.750	.672	.119	-.992	-.508	-6.313	31	.000
Pair 4	MASI at Enrolment - MASI 8 Weeks	2.0653	1.5145	.2677	1.5193	2.6114	7.714	31	.000
Pair 5	MASI at Enrolment - MASI 14 Weeks	2.9397	2.2101	.3907	2.1429	3.7365	7.524	31	.000
Pair 6	MASI at Enrolment - MASI 22 Weeks	3.0494	1.0395	.1838	2.6746	3.4242	16.59	31	.000

DISCUSSION

Despite tremendous research into the etiology, pathogenesis, and possible treatment options for melasma, the disease remains a therapeutic challenge to dermatologists, and a definitive modality of treatment is still a distant reality. Therapeutic armamentarium of melasma consists of hypo pigmenting agents, chemical peels, and lasers.[1] Peels are a well-known second line modality to remove excess epidermal pigment in the epidermal and mixed types of melasma, both as a sole treatment as well as an adjunct to other topical therapies. They act by thinning the stratum corneum, promoting epidermolysis, dispersing basal layer melanin, and increasing collagen genes expression. Although a number of new agents have come up, there is little published evidence supporting their use in day to-day practice and the choice becomes relatively limited when you are treating a patient with a Fitzpatrick skin type IV or above. Superficial peels which include glycolic acid, salicylic acid (SA), Jessner solution, and trichloroacetic acid (TCA) peels, with appropriate titration of concentrations are generally safe and efficacious for Fitzpatrick skin type IV to VI. [2,3]

There are very few objective published studies comparing the efficacy and safety of different chemical peels for melasma in type IV and V skin. This thesis aims to fill this void by evaluating the therapeutic response of melasma in Indian patients to glycolic acid (GA-35%) versus SM acid (20% salicylic/10% mandelic acid) versus phytic acid combination peel.

Our study included 96 patients with melasma. The mean age of the patients was 30.6 years. This is comparable to a study by Arun Achar & Rathi, which was 33.45 [6].

The average duration of the disease at the time of treatment was 2.03 years after the appearance of melasma. It is little early when compared to the study by Arun Achar & Rathi [6], which was 3.59 years.

The most common clinical type was centrofacial (63.5%) followed by malar (30.2%) & mandibular type was seen in only (4.2%) of the total patients. Centrofacial is considered to be the commonest type by various studies [16,26,56,71]. While in several Indian studies 57, malar type was found to be more common.

Majority of our patients were housewives (32%) and farmer (26%). About 63% of our patients attributed to sun exposure as a possible aggravating factor similar to another Indian study [6]. Positive family history was seen in 16.6% of our patients which is

little less compared to earlier studies where it varied from 20 -70% [58, 59]. Pathak et al [138] have suggested that genetics and UV exposure are the important factors in melasma.

Therapeutic response:

GA and SMA group showed relatively comparable results with 40% and 35% fall in MASI score at 14th week while 42% and 26% at 22nd week respectively. Different studies showing varying results, Sarkar et al [139] showed excellent results (>80% reduction) with 20% glycolic acid while Javaheri et al [140] shows only 47% reduction with 50% glycolic acid. In our study, MASI scores at 22 Weeks showed maximum reduction in glycolic acid acid group. Percentage reduction in MASI scored was lowest among phytic acid peel group with 22% reduction at 14 weeks and 23% reduction in 22 weeks.

In this study, we have reported that decrease in MASI score and VAS score at 8th, 14th, 22 weeks were significant within each group from baseline score but on comparing in between groups scores were comparable.

Glycolic acid peel is the most commonly used alpha hydroxy peel which has the smallest molecular weight and therefore is easily able to traverse the skin. It is extremely hydrophilic and has anti-inflammatory, keratolytic, and antioxidant effects. Unlike some other chemical peeling agents that pose a risk of hyper or hypopigmentation to darker skin types, GA peels as a 30% to 70% GA solution, can be used on all Fitzpatrick skin types I through VI, male or female, teens to adults. Side effects are substantially minimized when lower concentrations of 20% to 35% are used. [2] Higher concentrations often lead to irritation and may cause paradoxical hyperpigmentation in dark-skinned patients. It is time tested and has shown good response in epidermal and mixed type of melasma in Asian [4-7] and Black patients, mostly as a second-line agent. [8] A significant decrease in the MASI score from baseline to 12 weeks was observed in glycolic group with statistically significant results ($p < 0.001$).

The only side-effects observed with the GA peels were mild burning, erythema, desquamation, and a transient post inflammatory hyperpigmentation (PIH) which is a commonly observed side effect in darker phenotypes. It is known that epidermal-type melasma responds to GA peel, whereas dermal-type melasma does not, because of the deeper deposition of melanin in dermal type melasma and the inability of GA in the given concentration to reach that level. Increased incidence of PIH in group A could be explained by the presence of more patients with skin phototype V, who are more prone to PIH.

Salicylic-mandelic acid peel is a combination of an alpha hydroxy acid with a beta hydroxy acid.

Mandelic acid (MA), because of its large molecular weight (MW) tends to remain on the skin surface longer, penetrates stratum corneum slowly thus producing a uniform epidermal effect. It is associated with less stinging and burning as compared to the other lower-MW alpha hydroxy acid. It is an ideal peeling agent for sensitive skin and is well tolerated and more effective as compared to the traditional GA peels, in acne, post acne scarring, and pigment dyschromia's.[3,9]

Salicylic acid peels are well tolerated in all skin types (Fitzpatrick I to VI) and in all racial/ ethnic groups and are excellent peeling agents for numerous conditions including acne, melasma, and PIH in dark-skinned individuals. [2,8] Grimes [14] successfully demonstrated the efficacy and safety of 20% to 30% SA peel in patients of melasma with skin types V and VI, however, another randomized control split face trial found them to be ineffective in the treatment of melasma. [11] In this study, Phytic acid peel found comparable with other two groups in contrast with other studies in the past. SM peels were found to be as efficacious as GA in decreasing MASI score, were well-tolerated and better received by the patient. Salicylic-mandelic peels had better sustained efficacy and fewer side effects than GA, presumably due to greater lipophilicity of SA and larger molecular size of MA. However, mild transient burning sensation was noted in 25% of patients, which resolved in 1 to 2 days.

The phytic acid combination peel is a proprietary peel, made of a mixture of GA, lactic acid, MA, and phytic acid. Phytic acid combination peel has a slow release promoting continuous penetration of the skin, requires no external neutralization and therefore the danger of over peeling is avoided. It allows progressive and sequential actuation of its acid and is nonaggressive. Phytic acid (2%–4%) has proven to be efficient in the treatment of epidermal melasma, especially when associated with GA or retinoic acid. The typical burning sensation seen with the glycolic peel is not observed with the phytic acid peels. [12] There was a statistically significant reduction in MASI in glycolic acid group at the end of 14^{th} & 22^{nd} weeks and the results were rather more gratifying with GA and SM peels.

There are very few comparative studies of chemical peels in literature. In a split face comparative study for evaluation of efficacy of Jessner solution and 70% GA, both were found to work equally well in the treatment of melasma. [14] Khunger and colleagues [142] found no statistically significant difference in efficacy of 1% tretinoin as compared with 70%

glycolic peels. In a study to compare the efficacy and tolerance of TCA and GA in melasma, GA was found to be a better peeling agent. The response with TCA was rapid but unpredictable and was associated with local reactions and significant relapse rate, whereas response with GA was slower at onset, not associated with local reactions, and was more prolonged. [17]

In our study, we reported melasma percentage reduction at 14^{th} week, 22^{nd} week, physician general assessment as well as patient's general assessment among all the groups was statistically significant on comparison. However, the treatment related side effects like post inflammatory hyperpigmentation (6.2%), burning sensation (6.2%), and erythema (15.6%) in glycolic acid group that was found to be statistically significant compared with other treatment groups (SMA, and PA).

LIMITATIONS

1. There could be high lost to follow up patient's rate in our study because of inclusion of maximum patients from low socio-economic strata, for whom melasma was just a minor cosmetic impairment.
2. In this present study, we didn't perform or apply two methods of treatment on different sides of face of a patient which could have helped in better comparative analysis, and contrast with triple combination may have better demonstrated the efficacy of peels.
3. All the patients did not belong to the same Fitzpatrick type.
4. Outcome measures selected for this study were subjective (MASI); objective measures like narrowband reflectance spectrophotometer (mexameter) are more reproducible, and complement the subjective measures but are not available in this setting.
5. Most studies using peeling agents for melasma lack controls, blinding, and objective methods of evaluation, which causes difficulty in interpreting the results.
6. Glycolic acid peels used in this study were of relatively lower concentration.

In other Indian studies [143,144], authors have used up to 50% glycolic acid with efficacy in melasma. However Indian skin is sensitive and more prone to PIH and thus we chose to be on the safer side and used lower concentration of the peels. The presence of very few studies evaluating chemical peels is probably due to the fact that melasma is more prevalent in darker

complexioned individuals in whom there is a higher tendency for pigmentary changes to develop and thus the reluctance to perform these procedures. There are very few previous comparative studies between the above agents in melasma in Indian patients. However, we clearly observed that Phytic acid combination peel in our study is more effective than glycolic peels and Salicylic-mandelic acid peel in the reduction of the pigmentation in melasma in dark-skinned patients. Moreover, SM peel and GA peel seems to be comparable in this regard. Compared to GA peel, SM peel was found to be less irritating, better tolerated, and provided equivalent efficacy with maintained improvement during the follow-up.

Melasma is a common acquired pigmentary disorder in the dark skinned races. Cosmetic disfigurement associated with this condition imparts significant psychological distress. Although a variety of agents are available, it still remains a difficult condition to treat and to prevent recurrence. A thorough understanding of the risks and benefits of various therapeutic options is crucial in selecting the best treatment.

CONCLUSION

Treatment of melasma still remains challenging because of the prolonged duration of therapy. The substantial relapse rate, mainly attributed to inevitable persistence of the exacerbating factors (sun exposure) is still an obstacle.

In our study, glycolic acid is as effective as salicylic glycolic acid and more superior to the phytic acid combination in reduction of pigmentation in melasma in dark skinned patients. Further, randomized, controlled trials using new depigmenting agents, peeling agents, lasers, and other technologies are warranted to improve the management of this recalcitrant disorder. Superficial peels with appropriate titration of concentrations are generally safe and efficacious for darker skinned racial ethnic groups. However, in light of the labile responses of melanocytes of darker complexioned individuals, the clinician must always weigh the indication/necessity and benefit/risk ratio of the chemical peeling agent.

SUMMARY

Melasma is a common acquired pigmentary disorder in the dark skinned races. Cosmetic disfigurement associated with this condition imparts significant psychological distress. Although a variety of agents are available, it still remains a difficult condition to treat and to prevent recurrence. A thorough understanding of the risks and benefits of various therapeutic options is crucial in selecting the best treatment. There is paucity of literature comparing the efficacy of Glycolic acid, Salicylic-Mandelic acid, Phytic acid combination peels in melasma. We took up this thesis with following aims and objectives:

1. To study clinical profile of melasma patients using modified MASI score and Dermoscopy.

2. To study the effect of Glycolic acid, Salicylic-Mandelic acid and Phytic acid combination chemical peels in melasma.

We included all clinically diagnosed fresh cases of melasma of either sex of ≥ 18 years who agreed to undergo the procedure of chemical peels and who had given written consent were enrolled from the outpatient department of Santosh medical college & hospital, Ghaziabad and they were randomly divided into 3 groups consisting of 32 patient each group.

In this study we observed:

Melasma was most common in females in the age group of 30-32 years.

Male to female ratio with melasma in our study was (15.6%) and (84.4%) respectively.

The most common precipitating factor was sun exposure seen in 63% cases.

The mean age of all the Melasma patient in study is 30.55 ±5.96 years. The mean age of Melasma patients in Glycolic acid treatment group is 31.28 ±6.36 years whereas the mean age of the melasma patients in Salicylic-Mandelic acid treatment group is 30.38 ±5.22. The mean age of the melasma patients in Phytic Acid combination is 30.00 ±6.34.

Majority of the patients i.e. 93(96.9%) were married out of total 96 patients.

Majority of melasma patients in this study were either housewife (32%) or farmer (27%).

The most common morphological pattern was centrofacial type 47 (52.22%) while mixed type 50 (55.55%) was the most common based on Woods lamp.

Mean Value of Visual Analogue Scale (VAS) Scores of Melasma Patients varied at Various Time Points among three treatment groups in between (1 to 4). Least VAS score recorded among Phytic acid treatment group followed by Salicylic-Mandelic acid treatment group and maximum among Glycolic acid treatment group. However, the difference was statistically non-significant on inter group comparison.

Percentage reduction of melasma at 14th week and 22nd weeks among Glycolic acid was 40% and 41.78%; in Salicylic-Mandelic acid group it was 35.69% and 26.81% while in Phytic acid combination treatment group this was observed to be maximum as 22 % and 23 % respectively**.** On comparison this came out to be statistically significant.

Physician Global Assessment Score for melasma reduction in Glycolic acid treatment group was 3.09 and in Salicylic-Mandelic acid group was 2.44 while in Phytic acid combination treatment group it was 2.97. On comparison this came out to be statistically significant.

Similarly, Patients Global Assessment score in Glycolic acid group was 3.03, in Salicylic-Mandelic acid group was 2.22 and in Phytic acid combination group was 2.72. On comparison this came out to be statistically significant.

BIBLIOGRAPHY

1. Nicolaidou E, Antoniou C Katsambas AD Origin, clinical presentation, and diagnosis of facial hypermelanoses. Dermatol Clin. 2007 Jul;25(3):321-6, viii
2. Sarkar R, Ailawadi, Garg S. Melasma in Men: A Review of Clinical, Etiological, and Management Issues. J Clin Aesthet Dermatol. 2018 Feb;11(2):53-59
3. Rendon M, Berneburg M, Arellano I, Picardo M. Treatment of melasma. J Am Acad Dermatol. 2006 May;54(5 Suppl 2):S272-81
4. Vázquez M, Maldonado H, Benmaman C, Sanchez JL Melasma in men. A clinical and histologic study. Int J Dermatol. 1988 Jan-Feb;27(1):25-7
5. Sarkar R, Garg VK, Sonthalia S, Gokhale N. Melasma update. Indian Dermatol OnlineJ.2014 Oct;5(4):426-35
6. Achar A, Rathi SK. Melasma: a clinico-epidemiological study of 312 cases. Indian J Dermatol. 2011 Jul;56(4):380-2
7. Sanchez NP, Pathak MA, Sato S, Fitzpatrick TB, Sanchez JL, Mihm MC Jr. Melasma: a clinical, light microscopic, ultrastructural, and immunofluorescence study. J Am Acad Dermatol. 1981 Jun;4(6):698-710
8. Guinot C, Cheffai S, Latreille J, Dhaoui MA, YoussefS, Jaber K, et al. Aggravating factors for melasma: aprospective study in 197 Tunisian patients. J EurAcad Dermatol Venereol. 2010;24(9):1060–9(PubMed PMID: 20202051).
9. Tamega Ade A, Miot LD, Bonfietti C, Gige TC,Marques ME, Miot HA. Clinical patterns and epi-demiological characteristics of facial melasma inBrazilian women. J Eur Acad Dermatol Venereol.2013;27(2):151–6(PubMed PMID: 22212073).
10. Mandry Pagan R, Sanchez JL. Mandibular melasma.P R Health Sci J. 2000;19(3):231–4(PubMed PMID:11076368).
10. Ritter CG, Fiss DV, Borges da Costa JA, de Carvalho RR, Bauermann G, Cestari TF. Extra-facial melasma:clinical, histopathological, and immunohisto-chemical case–control study. J Eur Acad DermatolVenereol. 2013;27(9):1088–94(PubMed PMID:22827850).
11. Hexsel D, Lacerda DA, Cavalcante AS, MachadoFilho CA, Kalil CL, Ayres EL, et al. Epidemiology ofmelasma in Brazilian patients: a multicenter study.Int J Dermatol. 2014;53(4):440–4(PubMed PMID:23967822).

12. Mishra SN, Dhurat RS, Deshpande DJ, Nayak CS.Diagnostic utility of dermatoscopy in hydro-quinone-induced exogenous ochronosis. Int J Der-matol. 2013;52(4):413–7(PubMed PMID:22348652).
13. Carla Tamler, Rosa Maria et al , Francisco Burnier Carlos Pereira1, Carlos Baptista Barcauí. .Classification of melasma by dermoscopy: comparative study with Wood's lamp. Surgical & Cosmetic Dermatology. (2009) 1;3: 115-119.
14. Grimes PE, Yamada N, Bhawan J. Light microscopic, immunohistochemical, and ultrastructural alterations in patients with melasma. Am J Dermatopathol. 2005;27(2):96–101(PubMed PMID:15798432).
15. Bagherani N, Gianfaldoni S, Smoller BR. An overview on melasma. J Pigment Disord. 2015;2(10):218.
16. Garcia A, Fulton JE Jr. The combination of glycolic acid and hydroquinone or kojic acid for the treatment of melasma and related conditions. Dermatol Surg. 1996 May;22(5):443-7
17. Sarkar R, Garg V, Bansal S, Sethi S, Gupta C. Comparative Evaluation of Efficacy and Tolerability of Glycolic Acid, Salicylic Mandelic Acid, and Phytic Acid Combination Peels in Melasma. Dermatol Surg. 2016 Mar;42(3):384-91
18. Moin A, Jabery Z, Fallah N. Prevalence and aware-ness of melasma during pregnancy. Int J Dermatol.2006;45(3):285–8(PubMed PMID: 16533230).
19. Rathore SP, Gupta S, Gupta V. Pattern and preva-lence of physiological cutaneous changes in preg-nancy: a study of 2000 antenatal women. Indian JDermatol Venereol Leprol. 2011;77(3):402(PubMed PMID: 21508591).
20. Werlinger KD, Guevara IL, Gonzalez CM, RinconET, Caetano R, Haley RW, et al. Prevalence ofself-diagnosed melasma among premenopausalLatino women in Dallas and Fort Worth, Tex. ArchDermatol. 2007;143(3):424–5(PubMed PMID:17372115).
21. Taylor SC. Epidemiology of skin diseases in ethnicpopulations. Dermatol Clin. 2003;21(4):601–7(PubMed PMID: 14717401).
22. Sanchez MR. Cutaneous diseases in Latinos. Der-matol Clin. 2003;21(4):689–97(PubMed PMID:14717409).
23. Parthasaradhi A, Al Gufai AF. The pattern of skindiseases in Hail Region, Saudi Arabia. Ann SaudiMed. 1998;18(6):558–61(PubMed PMID:17344753).

24. El-Essawi D, Musial JL, Hammad A, Lim HW. Asurvey of skin disease and skin-related issues in ArabAmericans. J Am Acad Dermatol. 2007;56(6):933–8(PubMed PMID: 17321004).
25. Hiletework M. Skin diseases seen in Kazanchishealth center. Ethiop Med J. 1998;36(4):245–54(PubMed PMID: 11957300).
26. Vazquez M, Maldonado H, Benmaman C, SanchezJL. Melasma in men. A clinical and histologic study.Int J Dermatol. 1988;27(1):25–7(PubMed PMID:3346120).
27. Sarkar R, Puri P, Jain RK, Singh A, Desai A. Melasmain men: a clinical, aetiological and histologicalstudy. J Eur Acad Dermatol Venereol.2010;24(7):768–72(PubMed PMID: 20015053).
28. Pichardo R, Vallejos Q, Feldman SR, Schulz MR,Verma A, Quandt SA, et al. The prevalence of mel-asma and its association with quality of life in adultmale Latino migrant workers. Int J Dermatol.2009;48(1):22–6(PubMed PMID: 19126046.Pubmed Central PMCID: 2621062).
29. Jo HY, Kim CK, Suh IB, Ryu SW, Ha KS, Kwon YG,et al. Co-localization of inducible nitric oxide syn-thase and phosphorylated Akt in the lesional skinsof patients with melasma. J Dermatol.2009;36(1):10–6(PubMed PMID: 19207431).
30. Seckin HY, Kalkan G, Bas Y, Akbas A, Onder Y,Ozyurt H, et al. Oxidative stress status in patientswith melasma. Cutan Ocular Toxicol.2014;33(3):212–7(PubMed PMID: 24147944).
31. Mahmoud BH, Ruvolo E, Hexsel CL, Liu Y, OwenMR, Kollias N, et al. Impact of long-wavelengthUVA and visible light on melanocompetent skin.J Invest Dermatol. 2010;130(8):2092–7(PubMedPMID: 20410914).
32. Duteil L, Cardot-Leccia N, Queille-Roussel C, Mau-bert Y, Harmelin Y, Boukari F, et al. Differences in visible light-induced pigmentation according towavelengths: a clinical and histological study incomparison with UVB exposure. Pigment Cell Melanoma Res. 2014;27(5):822–6(PubMed PMID:24888214).
33. Kang HY, Hwang JS, Lee JY, Ahn JH, Kim JY, Lee ES,et al. The dermal stem cell factor and c-kit areoverexpressed in melasma. Br J Dermatol.2006;154(6):1094–9(PubMed PMID: 16704639).
34. Kang HY, Suzuki I, Lee DJ, Ha J, Reiniche P, Aubert J,et al. Transcriptional profiling shows alteredexpression of wnt pathway- and lipidmetabolism-related genes as well as melanogene-sis-related genes in melasma. J Invest Dermatol.2011;131(8):1692–700(PubMed PMID: 21562572).

35. Kim JY, Lee TR, Lee AY. Reduced WIF-1 expressionstimulates skin hyperpigmentation in patients withmelasma. J Invest Dermatol. 2013;133(1):191–200(PubMed PMID: 22951732).
36. Kim EJ, Park HY, Yaar M, Gilchrest BA. Modulationof vascular endothelial growth factor receptors inmelanocytes. Exp Dermatol. 2005;14(8):625–33(PubMed PMID: 16026585).
37. Lee HI, Lim YY, Kim BJ, Kim MN, Min HJ, HwangJH, et al. Clinicopathologic efficacy of copper bro-mide plus/yellow laser (578 nm with 511 nm) fortreatment of melasma in Asian patients. DermatolSurg. 010;36(6):885–93(PubMed PMID:20482724).
38. Adalatkhah H, Sadeghi-bazargani H, Amini-sani N,Zeynizadeh S. Melasma and its association withdifferent types of nevi in women: a case–controlstudy. BMC Dermatol. 2008;8:3(Pubmed CentralPMCID: 2525625).
39. Handel AC, Lima PB, Tonolli VM, Miot LD, MiotHA. Risk factors for facial melasma in women: acase–controlstudy.BrJDermatol.2014;171(3):588–94(PubMed PMID: 24749693).
40. Ortonne JP, Arellano I, Berneburg M, Cestari T,Chan H, Grimes P, et al. A global survey of the roleof ultraviolet radiation and hormonal influences inthe development of melasma. J Eur Acad DermatolVenereol. 2009;23(11):1254–62(PubMed PMID:19486232).
41. Jang YH, Lee JY, Kang HY, Lee ES, Kim YC. Oestro-gen and progesterone receptor expression in melasma: an immunohistochemical analysis. J Eur AcadDermatol Venereol. 2010;24(11):1312–6(PubMedPMID: 20337826).
42. Tamega Ade A, Miot HA, Moco NP, Silva MG,Marques ME, Miot LD. Gene and protein expressionof oestrogen-beta and progesterone receptors infacial melasma and adjacent healthy skin inwomen. Int J Cosmet Sci. 2015;37(2):222–8(PubMed PMID: 25439299).
43. Lutfi RJ, Fridmanis M, Misiunas AL, Pafume O,Gonzalez EA, Villemur JA, et al. Association ofmelasma with thyroid autoimmunity and otherthyroidal abnormalities and their relationship tothe origin of the melasma. J Clin Endocrinol Metab.1985;61(1):28–31(PubMed PMID: 3923030).
44. Kang WH, Yoon KH, Lee ES, Kim J, Lee KB, Yim H,et al. Melasma: histopathological characteristics in56 Korean patients. Br J Dermatol.2002;146(2):228–37(PubMed PMID: 11903232).

45. Pandya AG, Hynan LS, Bhore R, Riley FC, GuevaraIL, Grimes P, et al. Reliability assessment and validation of the Melasma Area and Severity Index(MASI) and a new modified MASI scoring method.J Am Acad Dermatol. 2011;64(1):78–83, e1–2(PubMed PMID: 20398960).
46. Rodrigues M, Ayala-Cortes AS, Rodriguez-ArambulaA, Hynan LS, Pandya AG. Interpretability of themodified melasma area and severity index (mMASI).JAMA Dermatol. 2016;152(9):1051–2(PubMedPMID: 27144383).
47. Balkrishnan R, McMichael AJ, Camacho FT, SaltzbergF, Housman TS, Grummer S, et al. Development andvalidation of a health-related quality of life instru-ment for women with melasma. Br J Dermatol.2003;149(3):572–7(PubMed PMID: 14510991).
48. Sarkar R, Garg V, Bansal S, Sethi S, Gupta C. Com-parative evaluation of efficacy and tolerability ofglycolic acid, salicylic mandelic acid, and phyticacid combination peels in melasma. Dermatol Surg.2016;42(3):384–91(PubMed PMID: 26859648).
49. Mazurek K, Pierzchala E. Comparison of efficacy ofproducts containing azelaic acid in melasma treat-ment. J Cosmet Dermatol. 2016;15(3):269–82(PubMed PMID: 27028014).
50. Kim SJ, Park JY, Shibata T, Fujiwara R, Kang HY.Efficacy and possible mechanisms of topicaltranexamic acid in melasma. Clin Exp Dermatol.2016;41(5):480–5(PubMed PMID: 27135282).
51. Dayal S, Sahu P, Dua R. Combination of glycolicacid peel and topical 20% azelaic acid cream inmelasma patients: efficacy and improvement inquality of life. J Cosmet Dermatol. 2016;16(1):35–42(PubMed PMID: 27500896).
52. Shankar K, Godse K, Aurangabadkar S, Lahiri K,Mysore V, Ganjoo A, et al. Evidence-based treat-ment for melasma: expert opinion and a review.Dermatol Ther. 2014;4(2):165–86(Pubmed Central PMCID: 4257945).
53. Trelles MA, Velez M, Gold MH. The treatment of melasma with topical creams alone, CO2 fractional ablative resurfacing alone, or a combination of the two: A comparative study. J Drugs Dermatol. 2010;9:315–22.
54. Jeong SY, Shin JB, Yeo UC, Kim WS, Kim IH. Low-fluence Q-switched neodymium-doped yttrium aluminum garnet laser for melasma with pre- or post-treatment triple combination cream. Dermatol Surg. 2010;36:909–18.
55. Kimbrough-Green CK, Griffiths CE, Finkel LJ, Hamilton TA, Bulengo-Ransby SM, Ellis CN, et al. Topical retinoic acid (tretinoin) for melasma in black patients. Avehicle-controlled clinical trial. Arch Dermatol. 1994;130:727–33.

56. Pandya AG, Hynan LS, Rafia Bhore, Fransell Copeland Riley, Ian L, Guevara et al Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a
new modified MASI scoring method. J Am Acad Dermatol. 2011 Jan;64(1):78-83, 83.e1
57. Ponzio, Humberto Antônio; Cruz, Moema Flores. Accurary of the exam with Wood's lamp in the classification of chloasmas. An. bras. dermatol 1993.; 68(6): 325-8,
58. Edwards EA, Finklestein NA, Duntley SQ. Spectrophotometry of living human skin in the ultraviolet range. J Invest Dermatol. 1951 May;16(5):311-21.
59. Dogra S, Mittal A. Role of dermoscopy in the diagnosis of pigmentary dermatoses in skin of color. Pigment Int 2014;1:41-3
60. Nanjundaswamy BL, Joseph JM, Raghavendra KR. A clinico dermoscopic study of melasma in a tertiary care center. Pigment Int 2017;4:98-103.
61. Dharni R, Madke B, Singh AL. Correlation of clinicodermatoscopic and Wood's lamp findings in patients having melasma. Pigment Int 2018;5:91-5.
62. Garg VK, Sinha S, Sarkar R. Glycolic acid peels versus salicylic-mandelic acid peels in active acne vulgaris and post-acne scarring and hyperpigmentation: a comparative study. Dermatol Surg. 2009 Jan;35(1):59-65
63. Nourmohammadi Abadchi S, Fatemi Naeini F, Beheshtian E. Combination of Hydroquinone and Fractional CO2 Laser versus Hydroquinone Monotherapy in Melasma Treatment: A Randomized, Single-blinded, Split-face Clinical Trial. Indian J Dermatol. 2019;64(2):129-135.
64. Boukari F, Jourdan E, Fontas E, Montaudie H, Cas-tela E, Lacour JP, et al. Prevention of melasmarelapses with sunscreen combining protectionagainst UV and short wavelengths of visible light: aprospective randomized comparative trial. J AmAcad Dermatol. 2015;72(1):189–90 e1(PubMedPMID: 25443629).
65. Castanedo-Cazares JP, Hernandez-Blanco D, Car-los-Ortega B, Fuentes-Ahumada C, Torres-Alvarez B.Near-visible light and UV photoprotection in thetreatment of melasma: a double-blind randomizedtrial. Photodermatol Photoimmunol Photomed.2014;30(1):35–42(PubMed PMID: 24313385).
66. Vazquez M, Sanchez JL. The efficacy of abroad-spectrum sunscreen in the treatment ofmelasma. Cutis. 1983;32(1):92, 5–6(PubMedPMID: 6349944).
67. Gupta AK, Gover MD, Nouri K, Taylor S. The treat-ment of melasma: a review of clinical trials. J AmAcad Dermatol. 2006;55(6):1048–65(PubMedPMID: 17097400).

68. Monteiro RC, Kishore BN, Bhat RM, Sukumar D,Martis J, Ganesh HK. A comparative study of theefficacy of 4% hydroquinone vs 0.75% kojic acidcream in the treatment of facial melasma. Indian JDermatol. 2013;58(2):157(PubMed PMID:23716817. Pubmed Central PMCID: 3657227).

69. Deo KS, Dash KN, Sharma YK, Virmani NC, OberaiC. Kojic acid vis-a-vis its combinations withhydroquinone and betamethasone valerate in mel-asma: a randomized, single blind, comparativestudy of efficacy and safety. Indian J Dermatol.2013;58(4):281–5(PubMed PMID: 23918998.Pubmed Central PMCID: 3726874).

70. Griffiths CE, Finkel LJ, Ditre CM, Hamilton TA, EllisCN, Voorhees JJ. Topical tretinoin (retinoic acid)improves melasma. A vehicle-controlled, clinicaltrial. Br J Dermatol. 1993;129(4):415–21 (PubMedPMID: 8217756).

71. Kimbrough-Green CK, Griffiths CE, Finkel LJ, Hamil-ton TA, Bulengo-Ransby SM, Ellis CN, et al. Topicalretinoic acid (tretinoin) for melasma in black patients.A vehicle-controlled clinical trial. Arch Dermatol.1994;130(6):727–33(PubMed PMID: 8002642).

72. Huh SY, Shin JW, Na JI, Huh CH, Youn SW, ParkKC. The efficacy and safety of 4-n-butylresorcinol 0.1% cream for the treatment of melasma: a ran-domized controlled split-face trial. Ann Dermatol.2010; 22(1):21–5 (PubMed PMID: 20548876.Pubmed Central PMCID: 2883392).

73. Fabbrocini G, De Vita V, Fardella N, Pastore F,Annunziata MC, Mauriello MC, et al. Skin needlingto enhance depigmenting serum penetration in thetreatment of melasma. Plastic Surg Int.2011;158241 (PubMed PMID: 22567235. PubmedCentral PMCID: 3335478).

74. Bagherani N, Smoller BR. Efficacy of topical tranexmicacid in the treatment of melasma. Dermatol Ther.2016;29(6):389–90(PubMed PMID: 26799239).

75. Budamakuntla L, Loganathan E, Suresh DH, Shan-mugam S, Suryanarayan S, Dongare A, et al. A ran-domised, open-label, comparative study oftranexamic acid microinjections and tranexamicacid with microneedling in patients with melasma.J Cutan Aesthet Surg. 2013;6(3):139–43(PubMedPMID: 24163529. Pubmed Central PMCID:3800287).

76. Kanechorn Na Ayuthaya P, Niumphradit N,Manosroi A, Nakakes A. Topical 5% tranexamic acidfor the treatment of melasma in Asians: a dou-ble-blind randomized

controlled clinical trial.J Cosmet Laser Ther. 2012;14(3):150–4(PubMedPMID: 22506692).

77. Lee HC, Thng TG, Goh CL. Oral tranexamic acid(TA) in the treatment of melasma: a retrospectiveanalysis. J Am Acad Dermatol. 2016;75(2):385–92(PubMed PMID: 27206758).

78. Wu S, Shi H, Wu H, Yan S, Guo J, Sun Y, et al.Treatment of melasma with oral administration of tranexamic acid. Aesthetic Plast Surg.2012;36(4):964–70(PubMed PMID: 22552446).

79. Bagherani N. Efficacy of topical flutamide in thetreatment of melasma. Dermatol Ther.2016;29(5):297(PubMed PMID: 27712039).

80. Alexis AF, Blackcloud P. Natural ingredients for darker skin types: growing options for hyperpig-mentation. J Drugs Dermatol JDD. 2013;12(9Suppl):s123–7(PubMed PMID: 24002160).

81. Lim JT. Treatment of melasma using kojic acid in agel containing hydroquinone and glycolic acid.Dermat Surg. 1999;25(4):282–4(PubMed PMID:10417583).

82. Kameyama K, Sakai C, Kondoh S, Yonemoto K,Nishiyama S, Tagawa M, et al. Inhibitory effect of magnesium L-ascorbyl-2-phosphate (VC-PMG) on melanogenesis in vitro and in vivo. J Am Acad Dermatol. 1996;34(1):29–33(PubMed PMID:8543691).

83. Espinal-Perez LE, Moncada B, Castanedo-Cazares JP.A double-blind randomized trial of 5% ascorbic acid vs. 4% hydroquinone in melasma. Int J Dermatol.2004;43(8):604–7(PubMed PMID: 15304189).

84. Costa A, Moises TA, Cordero T, Alves CR, MarmiroriJ. Association of emblica, licorice and belides as an alternative to hydroquinone in the clinical treat-ment of melasma. An Bras Dermatol.2010 ;85 (5): 613–20 (PubMed PMID: 21152784).

85. Kimball AB, Kaczvinsky JR, Li J, Robinson LR, MattsPJ, Berge CA, et al. Reduction in the appearance offacial hyperpigmentation after use of moisturizerswith a combination of topical niacinamide andN-acetyl glucosamine: results of a randomized,double-blind, vehicle-controlled trial. Br J Derma-tol. 2010;162(2):435–41(PubMed PMID:19845667).

86. Zhong SM, Sun N, Liu HX, Niu YQ, Wu Y. Reduc-tion of facial pigmentation of melasma by topicallignin peroxidase: a novel fast-acting skin-lighten-ing agent. Exp Ther Med. 2015;9(2):341–4(PubMedPMID: 25574195. Pubmed Central PMCID:4280934).

87. Morag M, Nawrot J, Siatkowski I, Adamski Z,Fedorowicz T, Dawid-Pac R, et al. A double-blind,placebo-controlled randomized trial of Serratulaquinquefolia folium, a new source of beta-arbutin,in selected skin hyperpigmentations. J CosmetDermatol. 2015;14(3):185–90(PubMed PMID:26119285).

88. Kang WH, Chun SC, Lee S. Intermittent therapy formelasma in Asian patients with combined topicalagents (retinoic acid, hydroquinone and hydrocor-tisone): clinical and histological studies. J Dermatol.1998;25(9):587–96(PubMed PMID: 9798345).

89. Chan R, Park KC, Lee MH, Lee ES, Chang SE, LeowYH, et al. A randomized controlled trial of the effi-cacy and safety of a fixed triple combination (fluocinolone acetonide 0.01%, hydroquinone 4%,tretinoin 0.05%) compared with hydroquinone 4%cream in Asian patients with moderate to severe melasma. Br J Dermatol. 2008;159(3):697–703(PubMed PMID: 18616780).

90. Kauh YC, Zachian TF. Melasma. Adv Exp Med Biol.1999;455:491–9(PubMed PMID: 10599387).

91. Holme SA, Beattie PE, Fleming CJ. Cosmetic cam-ouflage advice improves quality of life. Br J Der-matol. 2002;147(5):946–9(PubMed PMID:12410705).

92. Ahmed AM, Lopez I, Perese F, Vasquez R, Hynan LS,Chong B, et al. A randomized, double-blinded,placebo-controlled trial of oral Polypodium leucoto-mosextract as an adjunct to sunscreen in thetreatment of melasma. JAMA Dermatol.2013;149(8):981–3(PubMed PMID: 23740292).

93. Choudhry SZ, Bhatia N, Ceilley R, Hougeir F,Lieberman R, Hamzavi I, et al. Role of oralPoly-podium leucotomosextract in dermatologic diseases:a review of the literature. J Drugs Dermatol.2014;13(2):148–53(PubMed PMID: 24509964).

94. Arjinpathana N, Asawanonda P. Glutathione as anoral whitening agent: a randomized, double-blind,placebo-controlled study. J Dermatol Treatm.2012;23(2):97–102(PubMed PMID: 20524875).

95. Jang WS, Lee CK, Kim BJ, Kim MN. Efficacy of694-nm Q-switched ruby fractional laser treatmentof melasma in female Korean patients. DermatolSurg. 2011;37(8):1133–40(PubMed PMID:21585597).

96. Katz TM, Glaich AS, Goldberg LH, Firoz BF, Dai T,Friedman PM. Treatment of melasma using frac-tional photothermolysis: a report of eight cases withlong-termfollow-up.DermatolSurg.2010;36(8):1273–80(PubMed PMID: 20666816).

97. Park JM, Tsao H, Tsao S. Combined use of intensepulsed light and Q-switched ruby laser for complexdyspigmentation among Asian patients. Lasers SurgMed. 2008;40(2):128–33(PubMed PMID:18306166).

98. Rokhsar CK, Fitzpatrick RE. The treatment of mel-asma with fractional photothermolysis: a pilotstudy. Dermatol Surg. 2005;31(12):1645–50(PubMed PMID: 16336881)

99. Wanitphakdeedecha R, Manuskiatti W, Siri-phukpong S, Chen TM. Treatment of melasmausing variable square pulse Er:YAG laser resurfacing.Dermatol Surg. 2009;35(3):475–81(discussion81–2. PubMed PMID: 19250309).

100. Mark G Rubin ; Dr. VInay Suraf; Chemical rejuvenation of the face and non facial areas in Asian skin ; 2003; page 7 – 17.

101. Stegman SJ , Comparative histologic study of effects of the three peeling agents and dermabrasion on normal and sundamaged skin; Aesthetic plast surg 1982 ; 6 ; 123 – 135. 102. Dolezal J . Trichloroacetic acid solutions and basuc pharmacy. Manual of chemical peels . Rubin M ed Philadelphia J. B. Lippincott 1995 : 112 – 114.

103. Monheit GD, Skin penetration ; An essential step before chemical peeling or laser resurfacing. Cosmet Dermatol 1996; 9 9 -14.

104. Brody HJ , Variations and comparisons in medium depth chemical peeling . J Dermatol Surg Oncol 1989; 15 953 -963.

105. Monheit GD. The Jessners` trichloroacetic acid peel . Dermatol clin 1995: 13 (2) 277 – 283.

106. Matarasso SL , Glogau RG Chemical face peels, dermatol clin 1991 – 9 ; 131 -121.

107. Rubin M Manual of chemical peels . Philadelphia ; J. B Lippincott, 1995 120 – 121.

108. Lawrence N,cox SE,Cockrell CJ et al.A comparison of efficacy and safety of Jessners solution and 35% Trichloro acetic acid Vs 5% fluorouracil in the treatment of wide spread facial actinic keratosis.Arch Dermatol 1995.131.176-181.

109. Turg Re, Bergfeld WR,Vidimos AT RemR Bll. a hydroxy acid-barred cosmetic procedure. Guidelines for patient management. Am J clin.Dermatol 2002 march april 1(2) 81-88.

110. Dermatol Nurs. 1998 Aug:10(4) 269-272. 308.Facial reyurenater : use of a teaching model in care planning Le RoyL.Jan Rer skin Research Itc.San Rose CA . USA 37. Int J Dermatol 2000; May 40 (5) 354 to 7.

111. Jawaher S.N., Handa. S. Kaur, Kumar. S.Safety and efficacy of Glycolic acid facial peel in Indian women with Melasma. Dermatol. Surgery 2002 May; 28 (5) 383 to 7.Al-

112. Waiz MM, Al-Sharqi-Al, Medium depth Chemical peels in the treatment of acne scars in dark skin individuals, Baghdad, Iraq.

113. Saraf V. Chemical rejuvenation of the face and non-facial areas in Asian skin. 2003 Page No.10.

114. Mark G. Rubin Manual of chemical peeling. Philedelphia, J.B.Lippincott 1995 – 34 -35.

115 .Mark G. Rubin, M.D., Manual of Chemical peeling, Philedelphia, J.B. Lippincott 1995.

116. Griffin.T., Van Scottt E.J. Use of pyruvic acid in the treatment of actinic keratosis; A clinical and histo -pathological study. Cutis 1991 – 47: 325 to 329.

117. Mark G. Rubin, Manual of chemical peeling, Philedelphia, J.P. Lippincott 1995 (Page 94 to 102).

118. Cosmetic Dermatology – Principles of Practice, Leslie Baumann: Mcgrawhill 2002 (Chapter 20: Page 175 to 177).

119. Kligman A. Results of a pilot study evaluating the compatibility of topical tretinoin in combination with glycolic acid. Cosmetic Dermatology 1993; 6: 10: 28-32.

120. Murad. H., Shamban A.T., Moy L.S, Moy. R.L. Study shows that acne improves with glycolic acid regimen. Cosmet Dermatol. 1992 5 (11).

121. Naomi Lawrence William, P. Coleman III. Superficial chemical peeling. Chapter VI. Page 45.

122. Moy L.S., Murad. H., Moy R.L. Superficial chemical peels, R.G., ed Cutaneous Surgery. Philadelphia, W.B., Saunders Co, 1994 (463 to 478).

123. Vinay Saraf, Chemical Rejuvenation of face and non-facial areas in Asian Skin 2003 (Page 30 to 33).

124. Newman. N., Newman. A., Moy L.S., Babapour. R., Harris A.G., Moy. A.L. Clinical improvement of Photo aged skin with 50% glycolic acid. A double blind vehicle Controlled study. Dermatol surgery 1996 22 (455 to 460).

125. Vedamurthy. M., Salicylic acid peels. Indian Journal of Dermatology, Venereology and Leprology, 2004 70 (136-138).

126. Mark G. Rubin, Manual of Chemical Peeling, Philadelphia, J.B. Lippincott, 1995 (131-141).
127. Laura.L.Root: A complete Guide to Microdermabrasion International Journal of Cosmetology Volume VI (2) Page 23-100.
128. Laura L.Root: A complete Guide to Microdermabrasion, Chapter V (Page 69 to 82).
129. www.surgery.org/public/procedures microdermabrasion.php American society for aesthetic plastic surgery.
130. Lyold RI. The use of microdermabrasion for acne ; a pilot study. Dermatol surgery 2001 Apr, 27 (4), 329 -31.
131. Murad Alam, Nayomi E.Omura., Jeffery. S., Dover, Kenneth. A., Amdt. Glycolic Acid peels compared to Microdermabrasion : A right left controlled trial of efficacy and patient satisfaction: Dermatological Surgery, Volume 28 (Page 475) June 2002, Issue VI.
132. Harrold J. Brody. Glycolic acid peels compared to microdermabrasion: Dermatological Surgery, Volume 28 Issue VII, July 2002.
133. Male Bhalla, and Guruwinder and Thami, Microdermabrasion: Reppraisal and Brief Review of Literature, Dermatological Surgery, Volume 32 (Page 809) June 2006 Issue VI.
134. Faghihi G, Taheri A, Shahmoradi Z, Nilforoushzadeh MA. Solution of Azelaic Acid (20%),Resorcinol (10%) and Phytic Acid (6%) Versus Glycolic Acid (50%) Peeling Agent in the Treatment of Female Patients with Facial Melasma. Adv Biomed Res. 2017;6:9.
135. Garg, Shimona; Thami, Gurvinder Pal; Bhalla, Mala; Kaur, Jasleen; Kumar, Anand. Comparative Efficacy of a 35% Glycolic Acid Peel Alone or in Combination With a 10% and20% Trichloroacetic Acid Spot Peel for Melasma. Dermatologic Surgery, (2019) 45(11), 1394–1400.
136. Nanda S, Grover C, Reddy BS. Efficacy of hydroquinone (2%) versus tretinoin (0.025%) as adjunct topical agents for chemical peeling in patients of melasma. Dermatol Surg. 2004;30:385–8.
137. Sahu P., Dayal S. Most worthwhile superficial chemical peel for melasma of skin of color: Authors' experience of glycolic, trichloroacetic acid, and lactic peel. *Dermatol. Ther*. 2021;34:e14693. doi: 10.1111/dth.14693.

138. Pathak MA, Fitzpatrick TB, Kraus EW. Usefulness of retinoic acid in the treatment of melasma. J Am Acad Dermatol 1986;15:894-9.
139. Sarkar R, Kaur C, Bhalla M, Kanwar AJ. The combination of glycolic acid peels with a topical regimen in the treatment of melasma in Dark-skinned patients: a comparative study. Dermatol Surg 2002;28:828-32.
140. Javaheri SM, Handa S, Kaur I, Kumar B. Safety and efficacy of glycolic acid facial peel in Indian women with melasma. Int J Dermatol 2001;40:354-7.
141. Khunger N, Sarkar R, Jain RK. Tretinoin peels versus glycolic acid peels in the treatment of Melasma in dark-skinned patients. Dermatol Surg. 2004 May;30(5):756-60; discussion 760. doi: 10.1111/j.1524-4725.2004.30212.x. PMID: 15099320.
142. Sanchez NP, Pathak MA, Sato S. Melasma: a clinical, light microscopic, ultrastructural, and immunofluorescence study. J Am Acad Dermatol 1981;4:698-709.
143. Kumari R, Thappa DM. Comparative study of trichloroacetic acid versus glycolic acid chemical peels in the treatment of melasma. Indian J Dermatol Venereol Leprol 2010;76:447.

CLINICAL PROFORMA (Annexure I)

Serial no: OPD/CR No:

Name: Age/sex:

Address: Phone no:

Marital Status: Occupation:

CLINICAL HISTORY:

- Presenting complaints
- Site of onset
- Duration
- Progression
- Distribution
- History of Previous topical therapy
- History of Consuming oral contraceptive pills (if female):
- History of similar complaints in the family
- History of sun exposure/photosensitivity
- History of any other systemic illness (Thyroid, diabetes mellitus, addison's disease etc)

EXAMINATION:

- General physical & systemic Examination

DERMATOLOGICAL EXAMINATION:

- Site of involvement : (L/R)/nose/forehead/temples/neck/hands
- Size
- Appearance of Lesion
- Clinical Classification : Epidermal/Dermal/Mixed

MODIFIED MASI SCORING :

TIME	REGIONS OF FACE	AREA (0-6)	DARKNESS (0-4)	TOTAL MODIFIED MASI SCORE
BASELINE	F (0.3) ML (0.3) MR (0.3) C (0.1)			
0 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
2 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
4 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
6 WEEK	F (0.3)			

	ML (0.3) MR (0.3) C (0.1)			
8 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
10 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
14 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
18 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			
22 WEEK	F (0.3) ML (0.3) MR (0.3) C (0.1)			

DERMOSCOPIC FINDINGS: (Colour of lesion ; light Brown/dark brown/grey/ blue grey, regular/ irregular pigment network, presence of talengiectasia's

TIME	COLOUR OF LESION (BROWN/DARK BROWN/GREY/BLUE GREY)	PIGMENT NETWORK (REGULAR/IRREGULAR)	PRESENCE OF TALENGIECTASIA
BASELINE			
0 WEEK			
2 WEEK			
4 WEEK			
6 WEEK			
8 WEEK			
10 WEEK			
14 WEEK			
18 WEEK			
22 WEEK			

VISUAL ANALOG SCALE : Worse, no change, poor (<30%), fair (31 - 60%), good (>60%).

- At time of enrolment :
- 0 week:
- 2 week:
- 4 week:
- 6 week:
- 8 week:
- 10 week:
- 14 week:
- 18 week:
- 22 week:

INVESTIGATIONS:

- Thyroid function test (TSH/T3/T4) :
- Blood sugar (Fasting and PP) :

CONSENT FORM(Annexure II)

I .....S/D/W of .....

R/O.....

Hereby declare that I give my full, free, and voluntary informed consent to be a part of the thesis entitled " **Study of clinical profile and effect of Glycolic acid, Salicylic-Mandelic acid and Phytic acid combination chemical peels in melasma** " as case and I understand that this study will be used to investigate me/my relative. Dr. Sheraun Karira has informed me to my full satisfaction, in the language I understand, about the purpose and nature of the observational study carried out. I have been informed about the duration of the study, and instructions to be followed during the study period.

I give my full consent for being enrolled in the above study and I reserve my rights to withdraw from the study whenever I wish, without prejudice of my rights to undergo treatment at SANTOSH MEDICAL COLLEGE & Hospital, GHAZIABAD. I give my full consent and I don't have any issues in publication of this study.

Patient's Signature or left thumb impression

Name of Patient: Date:

We have witnessed that the patient has signed the above form in the presence of his/her free will after fully understanding its contents.

Signature of witness

Name:

Signature of investigator:

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Analysis address	drjyotibatra89.sug@analysis.urkund.com

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(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2022/1751[9] Dated: 05.08.2022

Subject: Grant of Ethical Clearance for Thesis Protocol Topic **"Study Of Clinical Profile And Effect Of Glycolic Acid, Salicylic-Mandelic Acid And Phytic Acid Combination Chemical Peels In Melasma"**, submitted by **Dr. Sheraun Karira,** MD/MS student of Batch 2020-2021, Department of **Dermatology**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"Study Of Clinical Profile And Effect Of Glycolic Acid, Salicylic-Mandelic Acid And Phytic Acid Combination Chemical Peels In Melasma", Dr. Sheraun Karira** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **22.07.2022** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[DR. ALPANA AGRAWAL]
REGISTRAR

Dr. Sheraun Karira,
MD/MS student of batch 2020-2021
Department of Dermatology
Email: sheraunkarira959@gmail.com

Copy to:
1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr. V.K.Garg (Guide)
7. HOD of **Dermatology**

MASTER CHART

S.NO	Treatment Type	Name	Age	Sex	Marital Status	Occupation	Melesma Clinical Type	Melesma Morphological Type	Fitzpatrick Skin Type	VAS Enrolme	VAS 2 wee	VAS 4 wee	VAS 6 wee	VAS 8 wee	VAS 10 we	VAS 14 we	VAS 18 we	VAS 22 we	MASI at Baseline	MASI at 2th weeks	MASI at 4th weeks	MASI at 6th weeks	MASI at 8th weeks	MASI at 10th weeks	MASI at 14th weeks	MASI at 18th weeks	MASI at 22th weeks	% of reduction at 14th weeks	% of reduction at 22nd weeks	Side effects	PHY. GA	PATIENTS GA	
1	Gly Acid	Anshul	28	M	Married	Engineer	centrofacial	epidermal	IV	1	2	3	3	4	5	4	4	4	21.9	20.9	18.5	15.9	15.5	13.2	12.9	8.7	8.7	41.1	60.3	NA	4	4	-78.1
2	Gly Acid	Rajesh	36	F	Married	housewife	malar	dermal/mixed	V	1	1	2	4	3	4	5	3	4	24.3	22.1	20.5	18.6	14.4	11.8	9.9	9.9	9.9	59.3	59.3	na	4	4	
3	Gly Acid	Parvathi	26	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	3	3	4	5	4	4	4	12.6	11.8	11.7	9.6	9.4	9.3	9	9	8.4	28.6	33.3	erythema	3	3	
4	Gly Acid	Manjula	29	F	Married	housewife	centrofacial	epidermal	IV	1	1	2	4	5	5	4	3	3	6.1	5.9	5.9	5.8	4.4	3.9	3.4	3.2	3.2	44.3	47.5	na	3	3	
5	Gly Acid	Sujatha	30	F	Married	farmer	centrofacial	dermal/mixed	V	1	2	2	3	4	4	4	4	4	17.4	17.2	17.1	16.8	14.2	13.1	12	10.5	9.6	31.0	44.8	na	3	3	
6	Gly Acid	Janaki	39	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	3	3	4	5	4	4	4	15.1	14.9	14.9	14.5	13	12.5	11.2	11.2	11.2	25.8	25.8	na	3	3	
7	Gly Acid	Nalini	28	F	Married	farmer	malar	epidermal	V	1	2	3	4	5	4	4	4	4	19.2	19.1	19	18	15	14.5	12.6	12	11.2	34.4	41.7	erythema	3	3	
8	Gly Acid	Selvi	32	F	Married	teacher	centrofacial	dermal/mixed	V	1	3	2	3	4	5	4	4	4	20.6	20	19.5	18.5	17	16.3	15.8	15.8	15.8	23.3	23.3	na	2	2	
9	Gly Acid	Madhavan	33	M	Married	farmer	centrofacial	epidermal	IV	1	3	2	3	4	5	4	4	4	12.6	12	11.5	9.2	9	8.7	8.4	8.4	8.4	33.3	33.3	na	3	3	
10	Gly Acid	Bhuvaneswari	30	F	Married	teacher	malar	epidermal	V	1	2	2	2	3	4	4	4	4	18.9	18.5	17	17.7	15	15	13.2	12.5	11.9	30.2	37.0	na	3	3	
11	Gly Acid	Noori	45	F	Married	housewife	centrofacial	dermal/mixed	V	1	1	2	3	4	5	5	4	4	20.7	20.5	19.9	19.5	16	15	14.1	13.5	12.9	31.9	37.7	na	3	3	
12	Gly Acid	Sankari	48	F	Married	housewife	malar	dermal/mixed	V	1	1	2	4	5	4	5	4	4	25.2	25	24.5	22.8	22	21.5	21.6	21.6	21.6	14.3	14.3	na	2	2	
13	Gly Acid	Manimala	34	F	Married	housewife	centrofacial	epidermal	III	1	2	3	4	4	4	4	3	3	18.9	16.5	12	8.6	7.5	6.6	5.7	5.7	5.7	69.8	69.8	na	4	5	
14	Gly Acid	Kalaivani	30	F	Married	farmer	centrofacial	dermal/mixed	V	1	1	2	3	4	4	4	4	4	20.4	20.4	20.4	20.4	18	15.5	14.2	14.2	14.2	30.4	30.4	na	3	3	
15	Gly Acid	Suganya	30	F	Married	housewife	centrofacial	dermal/mixed	IV	1	2	2	3	4	4	4	4	4	21.6	21.6	21.6	21.6	18	15.6	13.8	13.8	13.8	36.1	36.1	erythema	3	2	
16	Gly Acid	Rajeswari	21	F	Married	housewife	mandibular	epidermal	IV	1	2	2	3	3	3	4	4	4	3.2	3	2.9	2.8	2.5	2.5	1.8	1.8	1.8	43.8	43.8	na	3	3	
17	Gly Acid	Babyshalin	38	F	Married	farmer	centrofacial	dermal/mixed	V	1	2	3	4	4	5	4	4	4	22.8	22.8	22.8	22.8	18.5	16.8	15.6	15.6	15.6	31.6	31.6	burning sensation	3	3	
18	Gly Acid	Yasotha	34	F	Married	housewife	centrofacial	epidermal	IV	1	1	2	3	4	4	4	4	4	15.9	15.5	14.5	14.1	9.5	7.5	6.89	6.89	6.89	56.7	56.7	burning sensation	4	3	
19	Gly Acid	Vimala	35	F	Married	housewife	malar	dermal/mixed	V	1	2	2	2	3	4	4	3	3	14.4	14	13.9	13.4	11	11	8.2	8.2	8.2	43.1	43.1	na	3	3	
20	Gly Acid	Eswari	29	F	Married	housewife	centrofacial	dermal/mixed	V	1	3	3	3	4	3	3	3	3	15	15	15	15	13	12.2	10.5	10.5	10.5	30.0	30.0	PIH	3	3	
21	Gly Acid	Raji	21	F	Married	farmer	malar	dermal/mixed	V	1	2	3	3	4	3	3	3	3	10.8	9.5	8.8	7.8	6.5	5.8	4.8	5.6	7.2	55.6	33.3	PIH	3	2	
22	Gly Acid	Jenifer	27	F	Married	farmer	centrofacial	epidermal	IV	1	1	2	3	4	3	3	3	3	9	8	7.8	7.2	6.5	5.8	5.2	5.2	5.2	42.2	42.2	na	3	3	
23	Gly Acid	Arokiyam	28	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	2	2	3	4	4	4	18	17	14.6	13.5	12	11.5	10.38	10.38	10.38	42.3	42.3	na	3	3	
24	Gly Acid	Panchavarnam	24	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	2	2	3	3	3	3	12.3	12.3	12.3	12.3	10	9	6.7	6.7	6.7	45.5	45.5	na	3	3	
25	Gly Acid	Deepa	22	F	Married	housewife	malar	epidermal	III	1	3	3	4	4	3	3	3	3	14.4	11.3	10.5	7.6	6.5	6.1	5.6	5.6	5.6	61.1	61.1	na	4	4	
26	Gly Acid	Neetu	40	F	Married	housewife	malar	dermal/mixed	V	1	4	4	4	3	3	4	4	4	24.3	23.2	20	18.6	15.5	13.2	9.9	9.9	9.9	59.3	59.3	na	4	4	
27	Gly Acid	Jyoti	26	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	3	4	4	3	3	3	3	12.6	10.6	10	9.6	9.4	9.2	9	8.6	8.4	28.6	33.3	erythema	3	3	
28	Gly Acid	Priyanka	29	F	Married	housewife	centrofacial	epidermal	IV	1	2	2	1	3	4	3	3	3	6.1	5.9	5.8	5.8	4.5	3.8	3.4	3.3	3.2	44.3	47.5	na	3	3	
29	Gly Acid	Akanksha	30	F	Married	farmer	centrofacial	dermal/mixed	V	1	3	3	2	4	3	4	3	3	17.4	17	16.8	16.8	15	14	12	10.8	9.6	31.0	44.8	na	3	3	
30	Gly Acid	Sucharita	39	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	3	1	4	3	4	4	4	15.1	14.9	14.6	14.5	13.2	12.5	11.2	11.2	11.2	25.8	25.8	na	3	3	
31	Gly Acid	Shilpi	28	F	Married	farmer	malar	epidermal	V	1	3	3	4	3	3	3	4	4	19.2	19	18	18	16.5	14	12.6	11.8	11.2	34.4	41.7	erythema	3	3	
32	Gly Acid	Suman	32	F	Married	teacher	centrofacial	dermal/mixed	V	1	2	3	4	3	3	4	3	3	20.6	20.6	20.6	20.6	18	17.5	15.8	15.8	15.8	23.1	23.3	na	2	2	
1	SMA	Babli	40	F	Married	sister	centrofacial	dermal/mixed	3	1	2	2	3	3	4	4	3	3	27.73	25	23.5	21.1	18.5	17.83	17.83	16.5	15.3	35.7	44.8	na	3	3	
2	SMA	Rashmi	35	F	Married	sister	centrofacial	epidermal	5	1	3	3	4	5	3	4	4	4	19.15	18	17.5	14.85	12.5	11.9	11.8	10.5	9.8	38.4	48.8	erythema	4	3	
3	SMA	Sanjana	27	F	Married	house wife	malar	dermal/mixed	5	1	5	4	3	4	4	4	3	3	11.7	11	11	10.8	9.5	9	8.6	9	9.6	26.5	17.9	na	2	2	
4	SMA	Sathish	20	M	Married	student	malar	dermal/mixed	5	1	2	3	3	2	3	3	3	3	13.5	13	12.6	12.6	8	8	7.4	8.5	9.4	45.2	30.4	na	3	3	
5	SMA	Rajeswari	24	F	Married	house wife			4	1	3	3	4	4	3	3	3	2	12.8	10	10	8.8	7.7	7.7	6.8	7.2	7.4	46.9	42.2	na	3	3	
6	SMA	Prema	42	F	Married	house wife	centrofacial	epidermal	4	1	2	2	3	3	4	4	4	4	6.17	5	5	4.67	4	4	3.18	3.18	3.18	48.5	48.5	na	4	3	
7	SMA	Mohana	29	F	Married	clerk	centrofacial	dermal/mixed	5	1	3	3	4	4	4	4	3	3	15.6	15	14.4	14.4	12.8	12.8	12.8	12.8	12.8	17.9	17.9	na	2	2	
8	SMA	Dhanalakshmi	26	F	Married	farmer	malar	dermal/mixed	5	1	2	3	4	4	5	5	5	3	11.7	10.8	9.2	9.9	9.7	9.7	9	10.5	10.8	23.1	7.7	na	2	1	
9	SMA	Shanthi	30	F	Married	house wife	centrofacial	epidermal	4	1	3	3	4	4	4	4	4	3	13	12	10.5	7.66	7	7	6	6	6	53.8	53.8	na	4	3	
10	SMA	Chithra	39	F	Married	house wife	malar	dermal/mixed	4	1	3	3	4	5	5	4	4	4	14.15	13.5	12.5	12.5	11.5	9.5	7.57	7.5	7.2	46.5	49.1	na	4	3	
11	SMA	Sheeba	33	F	Married	farmer	malar	epidermal	5	1	4	4	3	5	5	3	3	3	12.1	12.1	10.9	10.9	10.5	10.5	9.14	10.5	10.48	24.5	13.4	na	2	2	
12	SMA	Sokkammal	30	F	Married	house wife	centrofacial	epidermal	4	1	4	4	2	5	3	2	2	2	6.8	6.8	6.8	6.8	5.6	5	4.5	4.5	4.5	33.8	33.8	na	3	3	
13	SMA	Malar	35	F	Married	teacher	centrofacial	dermal/mixed	3	1	2	3	3	3	2	2	2	1	14.39	13	13	12.25	8	8	7.9	8	8.55	45.1	40.6	na	3	3	
14	SMA	Selvi	33	F	Married	house wife	centrofacial	dermal/mixed	5	1	1	1	2	2	2	2	1	1	15.6	14	14	14.1	14.1	14.1	14.1	16.5	17.7	9.6	-13.5	na	0	0	
15	SMA	Sruthi	25	F	Married	house wife	centrofacial	epidermal	5	1	1	1	2	3	3	2	1	1	15.9	14	14	12.6	11	11	10.6	10.6	10.6	33.3	33.3	na	3	3	
16	SMA	Anitha	29	F	Married	farmer	malar	dermal/mixed	5	1	2	2	2	4	4	4	3	3	18	18	18	18	17	16.5	16.5	18.5	19.5	8.3	-8.3	na	0	0	
17	SMA	Mallika	32	F	Married	house wife	centrofacial	epidermal	4	1	3	3	3	3	3	2	2	2	13.8	18	11	10.8	10.8	10.8	10.8	11.6	12.5	45.5	38.9	na	3	3	
18	SMA	Aandal	35	F	Married	teacher	centrofacial	dermal/mixed	5	1	3	3	3	2	2	2	2	2	13.8	13.8	13.8	13.8	12.6	12.6	12.8	13.5	14.4	7.2	-4.3	PIH	0	0	
19	SMA	Saradha	29	F	Married	farmer	malar	epidermal	5	1	4	4	4	4	4	3	3	3	14.18	12.5	12	11.98	7	6.5	6.75	7	7.36	52.4	48.1	na	4	3	
20	SMA	Nagamani	31	F	Married	farmer	centrofacial	dermal/mixed	5	1	3	4	5	3	4	4	4	4	15.57	14	12	9.23	8.9	8.9	8.47	15	19.16	45.6	-23.1	na	0	0	
21	SMA	Rohini	26	F	Married	house wife	malar	dermal/mixed	5	1	3	3	3	2	2	2	1	1	24.12	20	18.5	17.63	18	18	18.69	19	19.28	22.5	20.1	na	2	2	
22	SMA	Velliyammal	35	F	Married	farmer	centrofacial	dermal/mixed	5	1	3	3	3	2	2	2	1	2	20.1	18.5	17	16.46	14	13.8	12.24	12.24	12.24	39.1	39.1	na	3	3	
23	SMA	Dharshini	23	F	Married	student	mandibular			1	2	3	4	3	3	3	2	1	15.9	15	14.8	12.32	9.6	9.8	9.68	9.68	9.68	39.1	39.1	na	3	3	
24	SMA	Vandhana	27	F	Married	farmer	centrofacial	dermal/mixed	5	1	2	3	4	5	4	4	4	3	28.55	26	19.8	17.15	16	16.2	16.14	18.5	19.78	43.5	30.7	na	3	3	
25	SMA	Devipriya	26	F	Married	house wife	centrofacial	dermal/mixed	5	1	3	3	3	4	3	3	2	2	28.55	24.8	23.5	17.15	16	16.3	16.14	18.5	19.78	43.5	30.7	na	3	3	
26	SMA	Shanvi	32	F	Married	house wife	centrofacial	epidermal	4	1	3	3	4	3	3	2	2	1	19.8	16.5	15.5	10.8	10.8	10.8	10.8	11.5	12.5	45.5	36.9	na	3	3	
27	SMA	Subhama	35	F	Married	teacher	centrofacial	dermal/mixed	5	1	2	2	2	2	2	2	1	1	19.8	13.8	13.8	13.8	13	12.8	12.8	13.5	14.4	7.2	-4.8	na	0	0	
28	SMA	Chandni	29	F	Married	farmer	malar	epidermal	5	1	3	3	4	3	3	3	3	1	14.18	13	12	11.98	10	9.8	6.75	7	7.36	52.4	48.1	rebound hyperpigmentation	4	3	
29	SMA	Anupama	31	F	Married	farmer	centrofacial	dermal/mixed	5	1	2	2	3	3	3	2	2	1	15.57	13	10.8	9.23	8.6	8.47	8.47	16	19.16	45.6	-23.1	na	0	0	
30	SMA	Kiran	26	F	Married	house wife	malar	dermal/mixed	5	1	3	3	4	5	3	3	3	2	24.12	24.5	20	17.63	18	18	18.69	17	19.28	22.5	20.1	na	2	2	
31	SMA	Jyoti	35	F	Married	farmer	centrofacial	dermal/mixed	5	1	2	3	4	4	3	3	3	2	20.1	18	18	16.46	13.8	13.8	12.24	12.24	12.24	39.1	39.1	na	3	3	
32	SMA	Manisha	23	F	Married	student	mandibular		4	1	2	3	4	4	3	3	2	3	15.9	14.6	14.6	12.32	10	10.8	9.68	9.68	9.68	39.1	39.1	na	3	3	
1	Phytic Acid	Ritu	21	F	Married	housewife	centrofacial	dermal/mixed	IV	1	2	2	1	1	2	1	1	1	21.6	21	20.5	19.8	19.8	19.6	19.6	19.2	18	9.3	16.7	erythema	3	2	
2	Phytic Acid	Madhu	38	F	Married	housewife	mandibular	epidermal	IV	1	2	2	2	2	1	2	2	2	3.2	3	2.8	2.8	2	2	1.8	1.8	1.8	43.8	43.8	na	3	3	
3	Phytic Acid	Sonali	34	F	Married	farmer	centrofacial	dermal/mixed	V	1	3	3	2	2	1	2	1	1	22.8	22.8	22.8	21	20	19.8	19.6	19	18	14.0	21.1	na	3	3	
4	Phytic Acid	Priyanka	45	F	Married	housewife	centrofacial	epidermal	IV	1	3	3	2	2	1	2	2	3	15.9	14.8	14.8	14.8	14.6	14	13.6	13	12	14.5	24.5	na	4	3	
5	Phytic Acid	Roopa	29	F	Married	housewife	malar	dermal/mixed	V	1	3	3	4	3	3	3	3	2	14.4	13.8	13.4	13.4	12.8	11.8	11.8	11.6	11	18.1	23.6	na	3	3	
6	Phytic Acid	Chandni	23	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	2	3	2	2	1	1	15	15	14.8	14.8	14.6	13	12.8	12.5	12	14.7	20.0	na	3	3	
7	Phytic Acid	Ayesha	27	F	Married	farmer	malar	dermal/mixed	V	1	2	3	4	5	3	3	2	2	10.8	9	8.5	7.8	7.8	7.6	7.4	7.4	7.2	31.5	33.3	na	3	2	
8	Phytic Acid	Noori	28	F	Married	farmer	centrofacial	epidermal	IV	1	2	2	3	4	4	3	1	1	9	8	7.5	7.2	7.2	7	6.9	6.8	6.8	22.2	24.4	na	3	3	
9	Phytic Acid	Khushi	24	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	3	4	3	3	2	2	18	17.2	17	16.8	16.8	16.4	16.2	16.2	16	10.0	11.1	na	3	3	
10	Phytic Acid	Riya	22	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	1	3	2	1	2	3	2	12.3	12.3	12.3	12	11.3	10.4	10.2	9.8	9.7	17.1	21.1	na	3	3	
11	Phytic Acid	Parmeet	40	F	Married	housewife	malar	epidermal	III	1	2	3	2	2	2	1	1	1	14.4	13	12.8	12.6	12.6	12.4	12.4	12.5	12	13.9	16.7	na	4	4	
12	Phytic Acid	Monica	26	F	Married	housewife	malar	dermal/mixed	V	1	2	2	3	1	2	3	2	2	24.3	24	18.9	18.6	15	13.8	9.9	18	20	59.3	17.7	na	4	4	
13	Phytic Acid	Geeta	29	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	3	2	1	3	2	2	12.6	10.8	9.8	9.6	9	9	9	8.8	8.4	28.6	33.3	na	3	3	
14	Phytic Acid	Reshma	30	F	Married	housewife	centrofacial	epidermal	IV	1	2	2	3	3	2	2	1	1	6.1	6	5.8	5.8	4.2	3.4	3.4	3.2	3.2	44.3	47.5	na	3	3	
15	Phytic Acid	Lakshmi	39	F	Married	farmer	centrofacial	dermal/mixed	V	1	2	3	4	2	2	3	4	3	17.4	17	16.8	16.8	15.8	15	14.8	14.6	14	14.9	19.5	na	3	3	
16	Phytic Acid	Meena	28	F	Married	housewife	centrofacial	dermal/mixed	V	1	2	2	2	2	3	2	2	2	15.1	14.8	14.5	14.5	14	13.8	12.9	12.8	12	14.6	20.5	na	3	3	
17	Phytic Acid	Neetu	32	F	Married	farmer	malar	epidermal	V	1	2	3	2	2	2	2	1	1	19.2	19	18.6	18	18	17	16.9	16.8	16.5	12.0	14.1	na	3	3	
18	Phytic Acid	Priti	27	F	Married	teacher	centrofacial	dermal/mixed	V	1	2	3	4	5	2	2	2	2	20.6	20.6	20.6	20.6	18.8	17.7	15.8	15.8	15.8	23.3	23.3	na	2	2	
19	Phytic Acid	Nishi	25	F	Unmarried	student	centrofacial	dermal/mixed	3	1	3	3	3	2	3	3	3	1	27.73	25.5	25	24.8	24.6	24.6	24	24	24	13.5	13.5	na	3	3	
20	Phytic Acid	Jennifer	27	F	Married	teacher	centrofacial	epidermal	5	1	2	2	3	2	2	2	2	2	19.15	18.9	18.8	18	17.8	17.6	17	17	16	11.2	16.4	na	4	3	
21	Phytic Acid	Babli	20	F	Married	house wife	malar	dermal/mixed	5	1	1	2	1	2	3	3	3	2	11.7	11	10.8	10.8	8.8	8.6	8.6	9.4	9.6	26.5	17.9	na	2	2	
22	Phytic Acid	Sanjay	24	M	Unmarried	student	malar	dermal/mixed	5	1	2	2	1	2	1	2	1	1	13.5	13	12.6	12.6	12.8	11.5	11	10.8	10.5	18.5	22.2	na	3	3	
23	Phytic Acid	Bhoori	42	F	Married	house wife			4	1	3	3	2	3	2	2	2	2	12.8	12.8	12.8	12.6	11	10	10	9.9	9.8	21.9	23.4	na	3	3	
24	Phytic Acid	Saima	29	F	Married	house wife	centrofacial	epidermal	4	1	2	3	2	3	2	2	1	1	6.17	5	4.9	4.67	3.5	3.5	3.18	3.18	3.18	48.5	48.5	na	4	3	
25	Phytic Acid	Shalini	26	F	Unmarried	clerk	centrofacial	dermal/mixed	5	1	3	4	2	2	3	3	3	3	15.6	15	14.8	14.4	13	12.8	12.8	12.8	12.8	17.9	17.9	na	2	2	
26	Phytic Acid	Heena	30	F	Married	farmer	malar	dermal/mixed	5	1	3	4	3	4	2	2	2	2	11.7	10.6	10	8.9	9.7	9	9	10	10.8	23.1	7.7	na	2	1	
27	Phytic Acid	Isra	39	F	Married	house wife	centrofacial	epidermal	4	1	2	2	3	4	3	3	2	2	13	12.8	12	12	11.9	11.8	11.6	11.5	11	10.8	15.4	na	4	3	
28	Phytic Acid	Nargis	33	F	Married	house wife	malar	dermal/mixed	4	1	2	2	3	4	3	3	2	2	14.15	13	12.8	12.5	12	12	11.7	11.2	17.3	20.8	na	4	3		
29	Phytic Acid	Meenu	30	F	Married	farmer	malar	epidermal	5	1	2	2	3	4	3	3	3	3	12.1	11.8	10.9	10.9	10.5	9.14	9.14	9.14	10.48	24.5	13.4	na	2	2	
30	Phytic Acid	Aishwarya	35	F	Married	house wife	centrofacial	epidermal	4	1	3	2	3	2	3	3	3	2	6.8	6.8	6.8	6.8	5	4.9	4.5	4.5	4.5	33.8	33.8	na	3	3	
31	Phytic Acid	Muskan	33	F	Married	teacher	centrofacial	dermal/mixed	3	1	3	2	3	3	3	3	3	1	14.39	13.5	12.9	12.25	12	11.6	11.3	11	8.55	21.5	40.6	na	3	3	
32	Phytic Acid	Wafa	25	F	Married	house wife	centrofacial	dermal/mixed	5	1	2	1	2	1	2	2	2	1	15.6	15	14.8	14.1	14.1	14.1	14.1	13.6	12.7	9.6	18.6	na	0	0	